The 29th World Congress on Controversies in Obstetrics, Gynecology & Infertility (COGI)

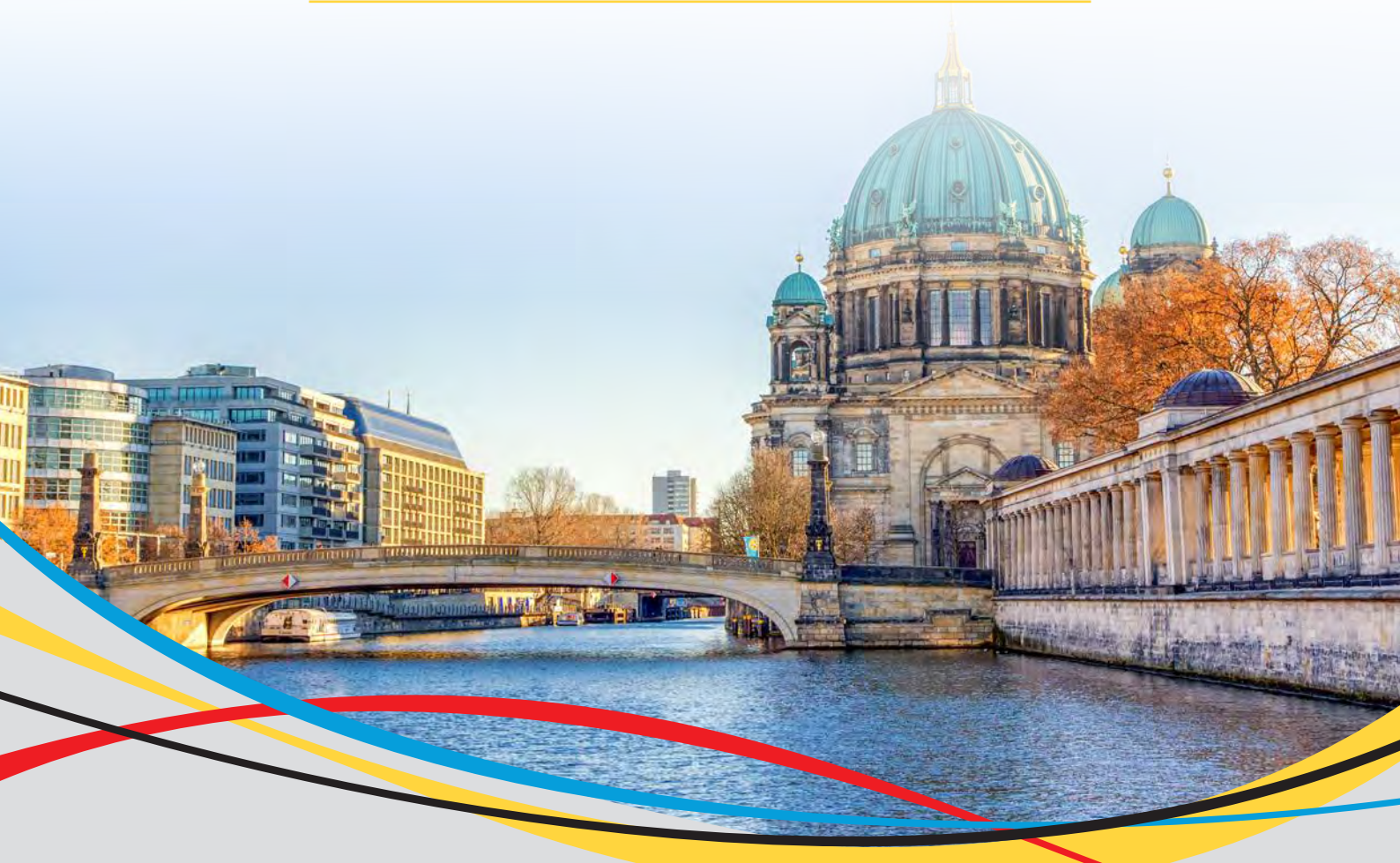
All About Women's Health

In partnership with Reproductive BioMedicine Online (RBMO)

December 2-4, 2021

BERLIN, GERMANY

Congress Program & Abstracts



www.cogi-congress.org

Timetable

THURSDAY, DECEMBER 2, 2021

	HALL A	HALL B
14:30-15:30	THE BEST OF RBMO 2020-2021	**14:00-16:45** LASER COURSE *Attendance by pre-registration only.* *First come-first served* *See pages 84, 85*
15:30-16:20	FROM INFERTILITY TO BIRTH	
16:20-17:50	PLENARY SESSION	
17:50-18:30	OPENING SESSION NOBEL PRIZE LAUREATE ROBERT G. EDWARDS ANNUAL LECTURE BEST ABSTRACT AWARDS ANNOUNCEMENT	
18:30-19:30	NETWORKING RECEPTION	

FRIDAY, DECEMBER 3, 2021

	HALL A	HALL B	HALL C
	INFERTILITY/ART/IVF	GYNECOLOGY	FETOMATERNAL MEDICINE
08:30-10:00	THE FUTURE OF IVF I	HRT AND CANCER	COVID 19
10:00-10:20	*Coffee break, visit the exhibition and poster viewing*		
10:20-11:50	THE FUTURE OF IVF II	INDUSTRY SUPPORTED SESSION *See page 86*	PRENATAL DIAGNOSIS
11:50-12:10	*Break*		
12:10-13:40	INDUSTRY SUPPORTED SESSION *See page 86*	VULVAR AND VAGINA	GESTATIONAL DIABETES MELLITUS (GDM)
13:40-14:30	*Lunch break, visit the exhibition and poster viewing*		
14:30-16:30	SURGICAL TREATMENT	PRESCRIBING HRT	ROUND TABLE DISCUSSION ON PRETERM LABOUR
16:30-16:50	*Coffee break, visit the exhibition and poster viewing*		
16:50-18:20	ISMAAR SESSION	GLOBAL HEALTH INITIATIVES IN GYNECOLOGICAL MALIGNANCIES	PERINATAL CHALLENGES

SATURDAY, DECEMBER 4, 2021

	HALL A	HALL B	HALL C
	INFERTILITY/ART/IVF	GYNECOLOGY	FETOMATERNAL MEDICINE
08:30-10:00	PCOS	ENDOMETRIAL CANCER	ULTRASOUND IN PREGNANCY
10:00-10:20	*Coffee break, visit the exhibition and poster viewing*		
10:20-11:50	CONTROVERSIAL ASPECTS ROUND ADD-ONS TO IVF, LABORATORIES AND CLINICAL PROCEDURES	WOMEN'S HEALTH AND WEALTH A PREIS SCHOOL ACADEMY SESSION	PRE-ECLAMPSIA TOXEMIA (PET) AND INTRAUTERINE GROWTH RETARDATION (IUGR)
11:50-12:00	*Break*		
12:00-13:30	ENDOMETRIOSIS ADENOMYOSIS	IN SEARCH OF NEW PERSPECTIVES: POI MAINLY DRIVEN BY GENETICS	LABOUR AND DELIVERY
13:30-14:20	*Lunch break, visit the exhibition and poster viewing*		
14:20-15:50	HORMONAL AND MORAL ASPECTS OF HUMAN FERTILITY	SLS: THE SOCIETY OF LAPAROENDOSCOPIC SURGEONS	INTRAPARTUM CARE (PART I)
15:50-16:00	*Coffee break, visit the exhibition and poster viewing*		
16:00-17:00	PREGNANCY LOSS	INDUSTRY SUPPORTED SESSION *See page 87*	INTRAPARTUM CARE (PART II)

Exhibition can be found on the foyer level as well as on the second floor

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Words of Welcome from COGI Chairpersons

Dear Colleagues,

COGI and **RBMO** are delighted to welcome you to the **29th World Congress on Controversies in Obstetrics, Gynecology and Infertility**.

Following the success of COGI 2020, which was fully digital and welcomed over 1000 delegates from all around the world, COGI will again welcome world renowned leaders in the field of Ob/Gyn and infertility, to review advances, breakthroughs and controversies in the field via round table discussions, debates, and lectures. Highlights will include the "Robert G. Edwards Nobel Prize Laureate" lecture, cutting edge "countercurrent" lectures by leading experts "who think differently", an inspiring fetomaternal medicine program, sessions on early prenatal diagnosis, pregnancy support, age-related risks, nutrition, the epidemic of multiple pregnancies, HPV, menopause, and more. As always, there will be ample time during every session for speaker-audience discussions.

In addition, we thank the next generation of physicians, scientists and researchers who have submitted abstracts for consideration for the Young Scientist Award.

Welcome to Berlin!

Sincerely,

COGI Congress Co-Chairpersons

Zion Ben Rafael
Israel

Bart C.J.M. Fauser
The Netherlands

Rene Frydman
France

Wolfgang Henrich
Germany

Jalid Sehouli
Germany

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Women's and Children's Health

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RESEARCH

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General Information

VENUE
Seminaris Campus Hotel
Takustraße 39
14195, Berlin

LANGUAGE
The official language of the congress in English.

COGI CONGRESS HOURS

Thursday, December 2	14:00-18:30
Friday, December 3	08:30-18:20
Saturday, December 4	08:30-17:00

CONGRESS ADMISSION – NAME BADGE
Admission to the scientific sessions, exhibition area and e-Posters is available to registered delegates only.

EXHIBITION OPENING HOURS (Foyer level and Second floor)

Thursday, December 2	18:30-19:30 (Networking session)
Friday, December 3	08:30-16:50
Saturday, December 4	08:30-16:00

POSTERS
All the posters are presented in electronic format. The e-posters are situated in the exhibition area on the second floor and online.

CERTIFICATE OF ATTENDANCE (non-CME/CPD)
Certificates of attendance will be sent by email after the congress to all registered delegates.

CME ACCREDITATION
The 29th COGI Congress has been accredited by the European Accreditation Council for Continued Medical Education (EACCME®) for a maximum of 16 CME credits (ECMEC®s).
To receive your CME accreditation certificate, please visit the congress website after the congress and complete the online form. The deadline to claim points is **December 20, 2021**. Your certificate will be sent to you approximately 60 days after completion of the survey.

LIABILITY AND INSURANCE
The COGI congress secretariat and the organizers cannot accept liability for personal accidents, loss or damage to private property, or any COVID 19 related loss, of participants, either during or directly arising from the 29th COGI Congress. Participants are advised to make their own arrangements with respect to health and travel insurance.

RECORDING POLICY
Recording (photographic, video and audio) of the session is strictly prohibited.

SOCIAL MEDIA
Follow COGI social media pages for the latest updates, key date reminders, and discussions with colleagues and experts from around the world.

- **COGI Congress**
- **Controversies in Obstetrics, Gynecology & Infertility (COGI)**
- **@cogicongress / #COGI**
- **www.instagram.com/cogi_congress**
- **cogicongress**

Notes

COGI

Scientific Program

THURSDAY, DECEMBER 2

14:30-15:30	THE BEST OF RBMO 2020-2021	HALL A
Capsule	The three best papers published in RBMO in 2020 are presented in this session	
Chairperson	**Bart Fauser**, *Netherlands*	
14:30-14:50	Drug-free in-vitro activation of follicles for infertility treatment in poor ovarian response patients with decreased ovarian reserve **Kazuhiro Kawamura**, *Japan*	
14:50-15:10	'There is only one thing that is truly important in an IVF lab: Everything' Cairo consensus guidelines on IVF culture conditions **Catherine Racowsky**, *USA*	
15:10-15:30	Organoids can be established reliably from cryopreserved biopsy catheter-derived endometrial tissue of infertile women **Bich Ngoc Bui**, *Netherlands*	

15:30-16:20	FROM INFERTILITY TO BIRTH	HALL A
Chairpersons	**Zion Ben Rafael**, *Israel* **Wolfgang Henrich**, *Germany*	
15:30-15:55	Nature to clinics: Paradigm shift. Embryo-maternal signaling **Eytan R. Barnea**, *USA*	
15:55-16:20	Fertility, pregnancy, and perinatal outcome among parents in the fourth and fifth decade of life. Pro and contra **Christian Dadak**, *Austria*	

16:20-17:50	PLENARY SESSION	HALL A
Capsule	What are the limits of IVF?	
Chairpersons	**Bart Fauser**, *Netherlands* **Zion Ben Rafael**, *Israel*	
16:20-16:40	*This talk will provide an overview of biosensors in medicine, with an emphasis on biosensing in the intrauterine environment* Biological sensors of in-utero monitoring **Ying Cheong**, *UK*	
16:40-16:50	Discussion	
16:50-17:10	*Human pluripotent stem cells are being used to model different aspects of human development from directed differentiation to a specific organ (in organoids) to models of gastrulation (in gastruloids) and blastocyst formation (blastoids). This field is moving forward very fast but remains highly controversial. I will review the relevant scientific developments as well as touch on potential ethical and legal implications.* Synthetic human entities with embryo-like features **Susana M. Chuva de Sousa Lopes**, *Netherlands*	

17:10-17:20	Discussion
17:20-17:40	*Recent efforts of understanding development of human embryos past implantation* Single cell analyses of human embryo development **Magdalena Zernicka-Goetz**, *UK*
17:40-17:50	Discussion

17:50-18:30	**OPENING SESSION**	**HALL A**
Chairpersons	**Zion Ben Rafael**, *Israel* **Bart Fauser**, *Netherlands* **Wolfgang Henrich**, *Germany*	
17:50-18:20	Nobel prize laureate Robert G. Edwards annual lecture *Recent efforts and challenges for growing mammalian embryos ex utero* Advanced artificial mammalian embryogenesis ex utero **Jacob Hanna**, *Israel*	
18:20-18:30	Best Abstract Awards	

18:30	**NETWORKING RECEPTION**

LASER COURSE

14:00-16:45	**LASER COURSE** ***See page 84, 85***	**HALL B**

INFERTILITY/ART/IVF

FRIDAY, DECEMBER 3

08:30-10:00	THE FUTURE OF IVF I	HALL A
Chairpersons	**Zion Ben Rafael**, *Israel* **Joyce Harper**, *UK*	
Capsule	Expanded genetic screening: The more we can, the more we spend - what is the limit?	
08:30-09:00 08:30 08:40 08:50	Debate: **Preparation: Should we be using expanded genetic screening in all patients?** Yes: **Rita Vassena**, *Spain* No: **Tessa Homfray**, *UK* Discussion	
Capsule	Stimulation remains a basic step in IVF, can we do better?	
09:00-09:30 09:00 09:10 09:20	Debate: **Stimulation: We should not use more than 150 units in most patients** Pro: **Frank Broekmans**, *Netherlands* Con: **Norbert Gleicher**, *USA* Discussion	
Capsule	Automation in IVF can improve the lab work and maybe decrease the cost	
09:30-10:00 09:30 09:40 09:50	Debate: **Automation in IVF** Automation in embryo culture: **Laura Rienzi**, *Italy* Automation in embryo freezing: **Amir Arav**, *Israel* Discussion	

10:00-10:20 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING **EXHIBITION AREA**

10:20-11:50	FUTURE OF IVF II	HALL A
Chairpersons	**Zion Ben Rafael**, *Israel* **Frank Broekmans**, *Netherlands*	
Capsule	Does biology limit PGT-A's ability to provide accurate information?	
10:20-10:40	Why the PGT-A hypothesis for biological reasons, simply, cannot work **Norbert Gleicher**, *USA*	
Capsule	The debate goes on, is PGT-A increase or decrease success?	
10:40-11:15 10:40 10:50 11:00	**HFEA recently downgraded PGT-A from "Amber" to "Red", suggesting it has no proof. Are we all in agreement?** Debate: **PGT-A – more harm than good?** Yes: **Sebastiaan Mastenbroek**, *Netherlands* No: **Tessa Homfray**, *UK* Discussion	
Capsule	HFEA claims that up to 74% of UK patients received some sort of add-ons - none of which received the HFEA "go ahead" light. Should we keep using these costly unproven methods?	
11:15-11:50 11:15 11:25 11:35	Debate: **Standard IVF vs add-on IVF – futile expense? What if the patient is willing to pay for add-ons?** Pro: **Scott Nelson**, *UK* Con: **Joyce Harper**, *UK* Discussion	

11:50-12:10 BREAK

12:10-13:10	INDUSTRY SUPPORTED SESSION *See page 86*	HALL A

13:10-13:40		HALL A
13:10-13:40	The new approaches with oral antagonist and new algorithm **Jacques Donnez**, *Belgium*	

13:40-14:30 LUNCH BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

14:30-16:30	SURGICAL TREATMENT	HALL A
Capsule	Controversial aspects of surgical procedures associated with IVF	
Chairperson	**Joop Laven**, *Netherlands*	
14:30-14:55	Update on Müllerian duct anomalies: Modern surgical approaches **Sara Brucker**, *Germany*	
14:55-15:40 14:55 15:10 15:25	Debate: **Cesarean scar defect: When to correct, by which method?** Pro hysteroscopy: **Eleonora Boschetti,** *Germany* Pro laparoscopy: **Olivier Donnez,** *Belgium* Discussion	
15:40-16:05	Fibroids must be treated prior to IVF? **Michelle Nisolle**, *Belgium*	
16:05-16:30	End of endometrial scratching? **Ben Mol**, *Australia*	

16:30-16:50 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

16:50-18:20	ISMAAR SESSION	HALL A
Capsule	Almost every novelty in IVF is met with skepticism	
Chairperson	**Geeta Nargund**, *UK*	
16:50-17:05	Natural and mild IVF - when and how to do it? **Geeta Nargund**, *UK*	
17:05-17:20	The microbiome - does it really matter to ART? **Joop Laven**, *Netherlands*	
17:20-17:50 17:20 17:30 17:40	Debate: **Duo-stim advantages and disadvantages** Pro: **Alberto Vaiarelli**, *Italy* Con: **Bart Fauser**, *Netherlands* Discussion	
17:50-18:20 17:50 18:00 18:20	Debate: **Freeze only strategy for all?** Con: **Ben Mol**, *Australia* Pro: **Human Fatemi**, *United Arab Emirates* Discussion	

INFERTILITY/ART/IVF

SATURDAY, DECEMBER 4

08:30-10:00	PCOS	HALL A
Capsule	The definition of PCO/PCOS has changed several times during the last 4 decades. Should we change it again? Despite our better understanding, the treatment remains a challenge	
Chairpersons	**Bart Fauser**, *Netherlands* **Ben Mol**, *Australia*	
08:30-08:55	PCOS: A brain disease? **Joop Laven**, *Netherlands*	
08:55-09:20	Defining the polycystic ovary: AMH or ultrasound? **Antonio La Marca**, *Italy*	
09:20-09:40	Does Cochrane reviews show any role for metformin in the management of PCOS? **Thomas Tang**, *UK*	
09:40-10:00	The hypo-androgenic PCOS-like phenotype at advanced ages, one of the most frequent causes of repeat IVF failure **Norbert Gleicher**, *USA*	

10:00-10:20 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

10:20-11:50	CONTROVERSIAL ASPECTS ROUND ADD-ONS TO IVF, LABORATORIES AND CLINICAL PROCEDURES	HALL A
Chairpersons	**Laura Rienzi**, *Italy* **Zion Ben Rafael**, *Israel* **Bart Fauser**, *Netherlands*	
Discussants	**Catherine Racowsky**, *France* **Norbert Gleicher**, *USA* **Antonio La Marca**, *Italy* **Joop Laven**, *Netherlands* **Verena Nordhoff**, *Germany*	
Lab procedures	• Perfect timings in the embryology lab: When to denude, when to fertilize, when to culture? • One or several culture media - which? • Noninvasive embryo selection • Genetic testing for donors	
Clinical procedures	• RIF - is there a valid definition? • Fresh versus frozen: What to prepare? • Optimal luteal support? • Aromatase inhibitors - when to use?	

11:50-12:00 BREAK

12:00-13:30	ENDOMETRIOSIS ADENOMYOSIS	HALL A
Capsule	The concept that uterine adenomyosis and pelvic endometriosis as well as endometriotic lesions at distant sites of the body share a common pathophysiology with endometriosis was promoted almost a decade ago. What is the current thinking?	
Chairpersons	**Zion Ben Rafael**, *Israel* **Olivier Donnez**, *Belgium*	
12:00-12:20	Adenomyosis and deep endometriosis: Two linked diseases? **Jacques Donnez**, *Belgium*	
12:20-12:40	Uterine adenomyosis: Can surgery help? **Leila Adamyan**, *Russia*	
12:40-13:10 12:40 12:50 13:00	Debate: **The endometrioma and the ovarian reserve: The challenge of the surgeon** To operate first: **Jacques Donnez**, *Belgium* ART before operation: **Edgardo Somigliana**, *Italy* Discussion	
13:10-13:30	Medical targets in endometriosis **Ludwig Kiesel**, *Germany*	

13:30-14:20 LUNCH BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

14:20-15:50	HORMONAL AND MORAL ASPECTS OF HUMAN FERTILITY	HALL A
Chairperson	**Edgardo Somigliana**, *Italy*	
14:20-14:40	The luteal phase in ART: Are we gaining ground? **Ben Mol**, *Australia*	
14:40-15:05	Women's biological clock, the molecular mechanisms **Jennifer Gruhn**, *Denmark*	
15:05-15:25	40 years of experience with the German IVF registry **Klaus Bühler**, *Germany*	
15:25-15:50	Does social egg freezing increase women's emancipation? **Guido Pennings**, *Belgium*	

15:50-16:00 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

16:00-17:00	PREGNANCY LOSS	HALL A
Capsule	Can we prevent pregnancy loss?	
Chairperson	**Matthias Korell**, *Germany*	
16:00-16:20	Prevention of pregnancy loss **Paul Piette**, *Belgium*	
16:20-16:40	Recurrent pregnancy loss (RPL) - what are the solutions? **Bettina Toth**, *Austria*	
16:40-17:00	Fertility surgery, myoma **Matthias Korell**, *Germany*	

GYNECOLOGY

FRIDAY, DECEMBER 3

08:30-10:00	HRT AND CANCER	HALL B
Capsule	Demystification of the relationship between HRT and cancer	
Chairpersons	**Santiago Palacios**, *Spain* **Sven O. Skouby**, *Denmark*	
08:30-09:00	Can HRT and treatment for menopause be individualized to reduce the incidence of breast cancer? **Mark Brincat**, *Malta*	
09:00-09:30	Breast cancer in special populations **Herjan Coelingh Bennink**, *Netherlands*	
09:30-10:00	HRT in cancer survivors **Pierluigi Benedetti Panici**, *Italy*	

10:00-10:20 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING **EXHIBITION AREA**

10:20-11:50	INDUSTRY SUPPORTED SESSION *See page 86*	HALL B

11:50-12:10 BREAK

12:10-13:40	VULVAR AND VAGINA	HALL B
Capsule	Longevity accentuates the need for better strategies for vulvar and vaginal atrophy	
Chairpersons	**Nick Panay**, *UK* **Sven O. Skouby**, *Denmark*	
12:10-12:30	Advances in anatomy and physiology of the vagina based on new treatments **Santiago Palacios**, *Spain*	
12:30-12:50	Vulvar pains and co-morbidities: Data from 1183 cases **Alessandra Graziottin**, *Italy*	
Capsule	Postmenopausal atrophy of the lower genital and urinary tract is distressing and requires new ideas to control symptoms	
12:50-13:20 12:50 13:00 13:10	Debate: **Is laser effective for treatment of Stress Urinary Incontinence** Yes: **Zdenko Vizintin**, *Slovenia* No: **Tim Hillard**, *UK* Discussion	
13:20-13:40	Translational medicine in reproductive ageing **Sven O. Skouby**, *Denmark*	

13:40-14:30 LUNCH BREAK, EXHIBITION, AND POSTER VIEWING **EXHIBITION AREA**

14:30-16:30	PRESCRIBING HRT	HALL B
Capsule	Balancing the benefits/risks of HRT will allow larger populations to enjoy HRT	
Chairpersons	**Mark Brincat**, *Malta* **Alessandra Graziottin**, *Italy*	
Capsule	The controversy surrounding androgen addition to HRT is ongoing	
14:30-15:00	Should androgens be routinely offered to optimize quality of life in menopause? **Alessandra Graziottin**, *Italy*	
15:00-15:30	Update on practical prescribing of new hormone therapy regimens **Nick Panay**, *UK*	
15:30-16:00	New strategies in the prevention of fragility fractures **Santiago Palacios**, *Spain*	
16:00-16:30	Use of HRT for cardiovascular prevention **Johannes Ott**, *Austria*	

16:30-16:50 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

16:50-18:20	GLOBAL HEALTH INITIATIVES IN GYNECOLOGICAL MALIGNANCIES	HALL B
Capsule	In 90 minutes around the world	
Chairpersons	**Sara Nasser**, *Germany* **Jalid Sehouli**, *Germany*	
16:50-16:55	Greetings and Introduction	
16:55-17:05	A wake-up call: Gynecological oncology on the global health agenda **Andreas Ullrich**, *Switzerland*	
17:05-17:15	20 years of gynecological capacity building in Cameroon through partnership **Patrick Petignant**, *Switzerland*	
17:15-17:20	Q & A	
17:20-17:30	Digital health as a driver for global women's health: The iSTARC and PARSGO vision **Sara Nasser**, *Germany*	
17:30-17:40	Patient advocacy groups in the MENA region **Joelle Abou Khalil**, *Lebanon-Sweden*	
17:40-17:50	Q & A	
17:50-18:00	Towards a global women's health taskforce **Jalid Sehouli**, *Germany*	
18:00-18:20	Panel Discussion: **Namory Keita**, *Guinea* **Basel Refky**, *Egypt* **Hind ElMalik**, *Qatar*	

GYNECOLOGY

SATURDAY, DECEMBER 4

08:30-10:00	ENDOMETRIAL CANCER	HALL B
Capsule	News, options and current barriers in the management of endometrial cancer	
Chairpersons	**Robert Armbrust**, *Germany* **Jalid Sehouli**, *Germany*	
08:30-09:00	Clinical implications of molecular diagnostics in endometrial cancer **Elena Braicu**, *Germany*	
09:00-09:30	Personalized surgical approach in endometrial cancer **Robert Armbrust**, *Germany*	
09:30-10:00	New options in medical therapy of advanced and relapsed endometrial cancer **Jalid Sehouli**, *Germany*	

10:00-10:20 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

10:20-11:50	WOMEN'S HEALTH AND WEALTH A PREIS SCHOOL ACADEMY SESSION	HALL B
Chairpersons	**Gian Carlo Di Renzo**, *Italy* **Nick Panay**, *UK*	
10:20-10:25	Welcome **Gian Carlo Di Renzo**, *Italy*	
10:25-10:35	The Welfare of Women (WoW) global health program endorsed by FIGO **Gian Carlo Di Renzo**, *Italy*	
10:35-10:50	Will body-identical MHT become the first choice for menopausal hormone therapy? **Vanadin Seifert-Klauss**, *Germany*	
10:50-11:05	Testosterone or not testosterone in menopause: That's the question! **Nick Panay**, *UK*	
11:05-11:20	Which progestogen to optimize breast and endometrial safety in MHT? **Ewald Boschitsch**, *Austria*	
11:20-11:50	Q & A	

11:50-12:00 BREAK

12:00-13:30	IN SEARCH OF NEW PERSPECTIVES: POI MAINLY DRIVEN BY GENETICS	HALL B
Capsule	Can better understanding lead to better solutions?	
Chairpersons	**Bart Fauser**, *Netherlands* **Nick Panay**, *UK*	
12:00-12:25	Is the ovary the mirror of longevity? **Micheline Misrahi**, *France*	
12:25-12:45	Genetic architecture of reproductive ageing **Felix Day**, *UK*	
12:45-13:05	FMR1 and the genetic control of folliculogenesis **Julia Rehnitz**, *Germany*	
13:05-13:30	Endo-ERN and POI **Luca Persani**, *Italy*	

13:30-14:20 LUNCH BREAK, EXHIBITION, AND POSTER VIEWING **EXHIBITION AREA**

14:20-15:50	SLS: THE SOCIETY OF LAPAROENDOSCOPIC SURGEONS	HALL B
Capsule	Surgical management of endometriosis depends on thorough understanding of the pathophysiology and anatomy	
Chairpersons	**Jessica Ybanez Morano**, *USA* **Mona Orady**, *USA*	
14:20-14:50	VNOTES: Vaginal Natural Orifice Transluminal Endoscopic Surgery **Jessica Ybanez Morano**, *USA*	
14:50-15:20	Pearls in endometrioma management **Mona Orady**, *USA*	
15:20-15:50	Robotics: A systematic approach to deep infiltrative endometriosis **Thiers Soares Raymundo**, *Brazil*	

15:50-16:00 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING

16:00-17:00	INDUSTRY SUPPORTED SESSION *See page 87*	HALL B

FETOMATERNAL MEDICINE

FRIDAY, DECEMBER 3

08:30-10:00	COVID 19	HALL C
Capsule	In the midst of this incredible pandemic, can we already draw initial conclusions?	
Chairpersons	**Gian Carlo Di Renzo**, *Italy* **Micheline Misrahi**, *France*	
08:30-08:45	Collateral damage of the COVID pandemic on pregnancy **Asma Khalil**, *UK*	
08:45-09:05	Vertical SARS-COV2 transmission support fetal/newborn resistance to infection **Eytan R. Barnea**, *USA*	
09:05-09:20	Effect of lockdown on premature birth **Ben Mol**, *Australia*	
09:20-09:40	Effect of COVID 19 on male fertility **Christopher Barratt**, *UK*	
09:40-10:00	Update on COVID-19 vaccination **Leif-Erik Sander**, *Germany*	

10:00-10:20 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING **EXHIBITION AREA**

10:20-11:50	PRENATAL DIAGNOSIS	HALL C
Capsule	Non-invasive and invasive prenatal diagnosis for all or by indication?	
Chairpersons	**Yariv Yogev**, *Israel* **Wolfgang Holzgreve**, *Germany*	
10:20-11:20 10:20 10:40 11:00	**cfDNA diagnostic or screening?** NIPD diagnostic indications: **Lyn Chitty**, *UK* Screening for aneuploidies and common genetic aberrations: **Caterina Bilardo**, *Netherlands* Discussion	
11:20-11:50	Non-invasive prenatal testing (NIPT) - ethical and legal issues, proper counseling is the key **Wolfgang Holzgreve**, *Germany*	

11:50-12:10 SHORT BREAK

12:10-13:40	GESTATIONAL DIABETES MELLITUS (GDM)	HALL C
Capsule	The clinical definition and management of this common complication of pregnancy , remain controversial	
Chairperson	**Gerard Visser**, *Netherlands*	
12:10-12:25	How to define well glycemic control? **Yariv Yogev**, *Israel*	
12:25-12:55 12:25 12:35 12:45	Debate: **Induction of labor for women with diabetes for all women at 38 weeks?** Yes: **Yariv Yogev**, *Israel* No: **Ute Schäfer-Graf**, *Germany* Discussion	
12:55-13:10	What is the best pharmacological therapy for GDM? (metformin\glyburide\insulin?) **Gerard Visser**, *Netherlands*	

13:10-13:40	Debate: **Should obese women be advised to lose weight in pregnancy?**
13:10	Yes: **Yariv Yogev**, *Israel*
13:20	No: **Alexander Weichert**, *Germany*
13:30	Discussion

13:40-14:30 LUNCH BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

14:30-16:30	**ROUND TABLE DISCUSSION ON PRETERM LABOUR**	**HALL C**
Capsule	Audience expert discussion of burning issues in perinatology	
Chairpersons	**Wolfgang Henrich**, *Germany* **Yariv Yogev**, *Israel*	
Discussants	**Diogo Ayres-de-Campos**, *Portugal* **Ute Schäfer-Graf**, *Germany* **Gerard Visser**, *Netherlands*	
	1. First trimester embryosonography before or after NIPT? 2. Detailed second trimester expert screening for everybody? 3. Induction of labor at 39 completed weeks for every pregnant woman? 4. How to induce women after previous C-section? 5. When and how to deliver twins? 6. Cervical length without or combined with biomarkers to predict prematurity 7. Is hospitalization necessary after preterm rupture of membrane? 8. How to use or combine progesterone, pessary and cerclage in the prevention of PTB? 9. How to manage adnexal masses in pregnancy? 10. What is the best technique to close the uterotomy during C-section?	

16:30-16:50 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

16:50-18:20	**PERINATAL CHALLENGES**	**HALL C**
Capsule	Hot controversies in perinatology	
Chairpersons	**Wolfgang Henrich**, *Germany* **Diogo Ayres-de-Campos**, *Portugal*	
16:50-17:05	The effect of antibiotics and environmental toxicants on placenta function and fetal growth **Gian Carlo Di Renzo**, *Italy*	
17:05-17:20	Is there a metabolic syndrome in pregnancy? **Yariv Yogev**, *Israel*	
17:20-17:35	Screening of HPV: Options and limits **Andreas Kaufmann**, *Germany*	
17:35-17:50	The role of secondary prevention in CMV - Valaciclovir, hyperimmune immunoglobulins **Max Hackelöer**, *Germany*	
17:50-18:05	Fetal-neonatal Rh disease eradication is still far to be completed in the world **Gian Carlo Di Renzo**, *Italy*	
18:05-18:20	Discussion	

FETOMATERNAL MEDICINE

SATURDAY, DECEMBER 4

08:30-10:00	ULTRASOUND IN PREGNANCY	HALL C
Capsule	High resolution ultrasound has become the leading tool in gestation and postpartum care. What are the limits?	
Chairpersons	**Wolfgang Henrich**, *Germany* **Larry Hinkson**, *Germany*	
08:30-08:55	1st trimester ultrasound screening **Rabih Chaoui**, *Germany*	
08:55-09:15	2nd trimester ultrasound screening **Stuart Campbell**, *UK*	
09:15-09:35	Ultrasound in the delivery room **Tullio Ghi**, *Italy*	
09:35-10:00	Ultrasound in the postpartum period **Wolfgang Henrich**, *Germany*	

10:00-10:20 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

10:20-11:50	PRE-ECLAMPSIA TOXEMIA (PET) AND INTRAUTERINE GROWTH RETARDATION (IUGR)	HALL C
Capsule	Can we predict and prevent pre-eclampsia toxemia (PET)?	
Chairperson	**Ute Schäfer-Graf**, *Germany*	
10:20-10:50	Value of preeclampsia screening: Do we need angiogenic factor? **Asma Khalil**, *UK*	
10:50-11:20	Correlation between placental weight and angiogenic marker in women with pre-eclampsia and IUGR **Lisa Dröge**, *Germany*	
11:20-11:50	The impact of sFlt/PlGF ratio on the prediction and management of preeclampsia **Luisa Pinto**, *Portugal*	

11:50-12:00 SHORT BREAK

12:00-13:30	LABOUR AND DELIVERY	HALL C
Capsule	All aspects for management during labor and delivery should be researched with adequately powered and designed to provide evidence-based guidance	
Chairpersons	**Asma Khalil**, *UK* **Larry Hinkson**, *Germany*	
12:00-12:30	Operative vaginal delivery should be forgotten? **Gerard Visser**, *Netherlands*	
12:30-13:00	Rotational forceps in the second stage of labour under ultrasound guidance **Larry Hinkson**, *Germany*	
13:00-13:30	Is peripartum cardiomyopathy an autoimmune disease? **Norbert Gleicher**, *USA*	

13:30-14:20 LUNCH BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

14:20-15:50	INTRAPARTUM CARE (PART I)	HALL C
Capsule	Women should have the opportunity to make informed decisions about their delivery. Physicians ought to be knowledgeable about the new subtleties of the various techniques	
Chairpersons	**Gerard Visser**, *Netherlands* **Diogo Ayres-de-Campos**, *Portugal*	
14:20-14:45	ST analysis: A false hope? **Diogo Ayres-de-Campos**, *Portugal*	
14:45-15:05	Fetal arrhythmias **Christoph Berg**, *Germany*	
15:05-15:30	Ultrasound in labor ward **Larry Hinkson**, *Germany*	
15:30-15:50	US external version in breech presentation **Larry Hinkson**, *Germany*	

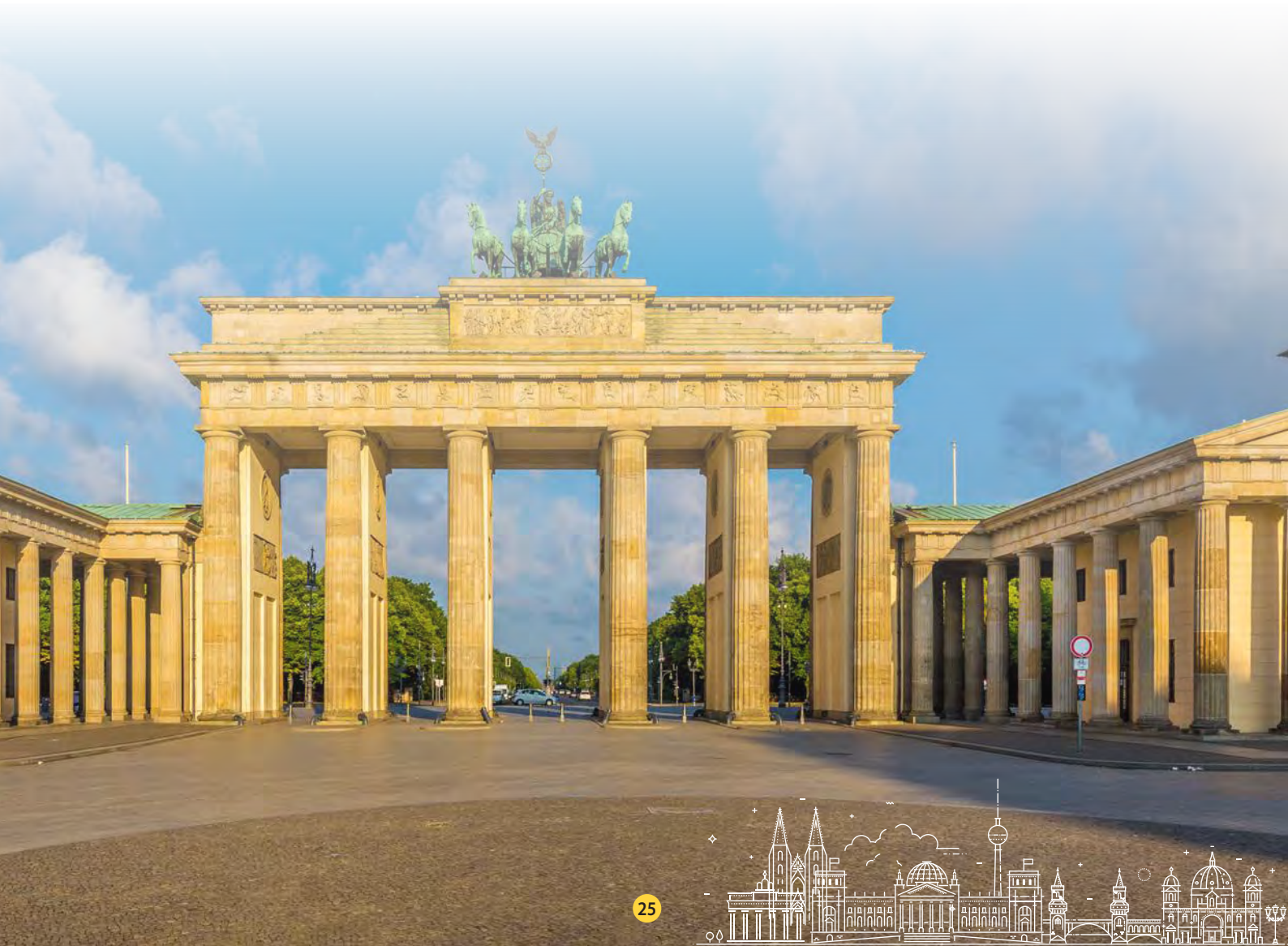
15:50-16:00 COFFEE BREAK, EXHIBITION, AND POSTER VIEWING EXHIBITION AREA

16:00-17:00	INTRAPARTUM CARE (PART II)	HALL C
Capsule	Women should have the opportunity to make informed decisions about their delivery. Physicians ought to be knowledgeable about the new subtleties of the various techniques	
Chairpersons	**Christoph Berg**, *Germany* **Larry Hinkson**, *Germany*	
16:00-16:20	Can arrested labor be predicted by early labor ultrasound? **Elvira Di Pasquo**, *Italy*	
16:20-16:40	Does intrapartum cardiotocography allow full maternal mobility? **Catarina Reis de Carvalho**, *Portugal*	
16:40-17:00	Do we need to use oxytocin in spontaneous labor? **Diogo Ayres-de-Campos**, *Portugal*	

Notes

COGI

Abstracts



SPEAKERS ABSTRACTS

PATIENT ADVOCACY GROUPS IN THE MENA REGION

Joelle Abou Khalil, *Founder of Matealda - Lebanon-Sweden*

This session will focus on patient advocacy groups in the MENA region specifically targeting gynecological cancer and address it from the perspective of patients and caregivers. We will present Matealda, a patient and caregiver community initiative in the region, as a case study and discuss the challenges being faced with but also highlight on the absence of other advocacy groups in the region because of these. They are often deeply rooted in the social and cultural status but also due to the unstable political and economic situation in the region. The lack of access to basic needs and medicine is part of the daily struggles in the MENA region. Adding to those, the lack of awareness and gathering of accurate data hinders the work of advocacy groups. Today many of these individuals and groups advocates such as Matealda are often left working alone with minimum support and with scarce resources. The individual commitment from patients, caregivers, volunteers and even doctors is what keeps them somewhat existing even if doing the minimum for the cancer patients but this doesn't really secure their sustainability in the long run. Patient advocacy groups play a vital role in serving as catalysts for improved communication and continuous support for all parties (doctors, medical staff, patients, caregivers, decisionmakers). They contribute to stronger and more reliable collaborations thus leading to better and equal health care for patients. If these patient advocacy groups are provided with the right tools and resources, they could serve as fully operating support system which today is more desirable than ever before for all parties involved. "Cancer is just a word, not a sentence" is often shared on various patient advocate platforms and it is true that we have come a long way in the medical field. We are able today to say that in many cases, cancer does not have to be associated with a death sentence. But the word itself is still difficult to even say out loud and for many it's considered a taboo, especially for women in the MENA region. In addition, to this we add to it the daily obstacles mentioned earlier which then results in priorities being made at the expense of these women's health. The only solution to overcome all these challenges and pave the way for patient advocacy groups to be more efficient is to provide them with a support system in form of a common platform. This should serve them on a local and regional level and at the same time provide them with continuous support from the global community. Matealda's vision to remain an advocate in the face of these challenges may started off as an individual initiative but is today raising the voice of many others. As a member of Pan-Arabic Research Society for Gynecological Cancer and i-STARC, we believe in coming together as one global health community to be able to provide that sustainable support in form of common platform.

RARE VERTICAL SARS-COV2 TRANSMISSION: EFFECTIVELY MEDIATED BY MATERNAL-INDUCED PROTECTION AND FETAL/NEWBORN RESISTANCE TO INFECTION

Eytan R. Barnea MD, FACOG, S.I.E.P, The Society for the Investigation of Early Pregnancy, NY, NY, USA. FIGO Safe Motherhood Newborn Health Committee member.
Nicoletta Di Simone, *Department of woman and child health and public health, A Gemelli, University Hospital Foundation IRCCS, Italy*, Current address: *of Biomedical Sciences, Humanitas University, IRCCS, Humanitas Research Hospital, Italy*
Simonetta Costa, *Department of woman and child health and public health, A Gemelli, University Hospital Foundation IRCCS, Italy*
Paola Cattani, *Laboratory of microbiology, A Gemelli, University Hospital Foundation IRCCS, Italy*
Giovanni Scambia, *Department of woman and child health and public health, A Gemelli, University Hospital Foundation IRCCS, Italy*
Gianni Vento, *Department of woman and child health and public health, A Gemelli, University Hospital Foundation IRCCS, Italy*
Maurizio Sanguinetti, *Laboratory of microbiology, A Gemelli, University Hospital Foundation IRCCS, Italy*.

Problem: Following maternal exposure to bacterial/viral infection fetal disease may/may not develop despite maternal disease severity. If the fetus/newborn is compromised it may also be independent whether an active fetal infection is present. Herein maternal-SARS-COV2 infection heterogeneity / fetal exposure/response, antibody transfer is critically analyzed. Further the positive impact of maternal vaccination is analyzed -where IgG is transmitted after 16 weeks gestation. ***Methods:*** Delineate SARS-COV2 vertical transmission (VT) continuum from conception until post-delivery. Address high maternal vulnerability, placenta/membrane infection vs minimal VT- reflecting innate fetal resilience. ***Results:*** Current evidence and the cause of limited VT are due to 1. SARS-COV2+ maternal infection or in vaccinated patients' the implantation and pregnancy rate are not affected. 2. URI is rarely systemic, while patients with co-morbidities, diabetes, cardiac, vascular, coagulation- are promptly delivered, and/or receive antivirals /antibiotics /steroids /anticoagulants. They may also require ICU. However, the access is limited in low/medium resource countries causing significant VT-independent maternal death and IUFD. 3. Sources of VT: Mostly by hematogenous spread via virus and/or infected immune cells causing placental villitis and fetal compromise without active fetal infection. Infection is rarely transmitted through semen, amniotic fluid, or breast milk. 4. Placental ACE2 protein (virus spike receptor) expression is low at term, but placental surface is large, therefore local immunity can shield and/or facilitate VT. 5. Minimal VT rates reflect local fetal resilience despite the high ACE-2 receptors presence in lung, liver, and heart- which is counteracted by the maturing local immune system-prepared for post-natal life. 6.Even with mild maternal infection, protective anti-SARS2-Cov2 IgG is transmitted to the fetus, preventing VT. 7. Infected newborn frequently appears healthy however, to document infection IgM requires >4 days to develop and need to be confirmed by IgG >2 weeks-whether such an IgG does persist in the newborn is unknown. 8. PCR viral test uses nasal/rectal/ocular swab not-blood however transmission is transplacental-low virus titers. 9.Peripartum/intrapartum/postpartum infection newborn/patient/family/staff are not tested unless symptomatic-real infection rate by VT or it is horizontal remains unknown. 10. Newborn can be breast-fed (milk is safe) lead to transfer of protective antibodies. 11.At the Gemelli Hospital a total of 42 SARS-COV2 infected pregnant patients participated in this study, some had severe disease. Only 2 newborns had a documented VT one following vaginal the other by C/S delivery (tested by nasopharyngeal RTPCR, both newborns had Apgar 8). 12. Large studies from US, and India, despite severe maternal disease similarly confirm minimal VT although in some cases leading up to maternal death and IUFD. 13. Viral variants infectivity continue to increase leading to high maternal morbidity/mortality (mostly in unvaccinated patients) which perforce cause fetal death independent of VT unless prompt delivery. 14. Did previously infected patients acquire natural immunity? Whether vaccination/booster is needed is debated. Both antibody titers and cellular immunity currently is not tested prior to vaccination. 15. Vaccination debate Y/N continues despite documented safety/protection and evolving viral mutants which increase infection rate and associated pathology. 16. Finally: SARS2-COV2 IgG vaccine is effective/safe and transmits protective maternal antibodies to the fetus. ***Conclusion:*** CALL TO ACTION: Minimize infection spread, vaccinate prior/during pregnancy since in both times it is safe/protective. Improve VT detection use PCR to check placenta, confirm in newborn (pharynx, ocular, rectal) and

IgG blood titer. Develop sensitive blood tests to determine virus titer which is imperative given long-term COVID-19 concern (cardiac, neurologic) since children can be affected, and spread the infection. Apply lessons learnt from other rare beta-corona infections (SARS-COV/MERS) which could help given the ongoing virus mutations which increase disease severity. Overall, due to prompt/improved maternal management, maternal IgG transfer, innate fetal resilience, and expanding vaccination rates the VT rate in COV-19 is expected to remain low. Further most infected newborn is only mildly symptomatic rarely requiring ICU, but hospitalization length is prolonged and long-term prognosis remains uncertain.

FETAL ARRHYTHMIAS

Prof. Dr. Christoph Berg, *Leiter Fetalchirurgie Universitätsfrauenklinik Bonn; Leiter Pränatale Medizin Universitätsfrauenklinik Köln; Leiter Pränatale Medizin Marienhospital Witten, Germany*

Arrhythmias are the most common cardiac anomalies in the intrauterine period. They are classified as irregular beats, bradyarrhythmia and tachyarrhythmia. Although 90% of fetal arrhythmias are paroxysmal ectopic beats and are well tolerated by the fetus, some rarer arrhythmias may lead to intrauterine cardiac failure and hydrops. A subset of affected fetuses profits from intrauterine treatment, while in others the benefit of intrauterine treatment remains questionable. However, the majority of arrhythmias do not warrant intrauterine treatment, in contrary, it would even be harmful. Therefore, an accurate diagnosis is warranted in all cases of fetal rhythm disturbance. This lecture will give an overview on all types of fetal arrythmia, the diagnostic pathway as well as the therapeutic options if intervention is necessary.

WHICH PROGESTOGEN TO OPTIMIZE BREAST AND ENDOMETRIAL SAFETY IN MHT?

Ewald Boschitsch, *KLIMAX Menopause and Osteoporosis Clinic, Vienna, Austria*

Safety in menopause hormone therapy (MHT) has been studied extensively in the past 20 years. In particular, the type of progestogen has been suggested to have major impact on the risk for breast cancer and some impact on the risk for endometrial pathologies. In many studies significant differences were found between synthetic progestogens, also called progestins, and micronized progesterone (P4), which is identical to the body's natural hormone synthesized by the ovaries. In general, MHT containing P4 was not associated with an increased risk for breast cancer when compared to non-use of MHT, and the risk was significantly lower than with MHT containing progestins. On the other hand, data of some studies propose a higher rate of insufficient endometrial protection and potentially decreased safety when MHT is combined with P4 than with progestins. We searched our database for both, terms related to breast- and to endometrial pathologies in patients who received P4, mostly combined with transdermal estradiol, to see if our real-world data agree with data of controlled trials. The results of this retrospective data evaluation will be presented as well as monitoring and risk reducing management measures will be discussed to optimize safety in clinical practice of MHT.

CAN HRT AND TREATMENT FOR MENOPAUSE BE INDIVIDUALISED TO REDUCE THE INCIDENCE OF BREAST CANCER?

Prof Mark Brincat. UOM, QMUL.
MRCS, LRCP, FRCOG, PhD(Lond), FRCPI

In its broadest sense, Hormone Replacement Therapy (HRT) includes other steroids such as SERMS and TSECS that have been developed. The major challenge has been on how to interpret data from the NIH study, the WHI whose first publication was in JAMA 2001. Since that first publication, a number of follow-up papers from that study have clarified certain issues. The Conjugated Oestrogen (E) only arm of the study had from the start shown suggestion that there was a reduction in Breast Cancer cases compared to the Combined E+P group and to the placebo group. In an update of the study, published in 2017, with an 18 year follow-up, there was a 44% lower incidence of Breast Cancer deaths in the women on the Oestrogen only arms who had been on Conjugated Oestrogens (E) for around 7 years, since that group was allowed to proceed further until it too was stopped.
Other agents used at the time of the Menopause such as the SERM, Raloxifene 60mgs daily has also been shown in at least three major studies to reduce the incidence of oestrogen receptor breast cancer cases by as much as 50%. The same applies for other pharmaceuticals such as Vit D and statins which are sometimes used as incidental treatment for other conditions prevalent the time of the Menopause. Ongoing, but promising studies are on Oestetrol (E4) currently being concluded and on Bazedoxifene another SERM. The HRT and Breast Cancer relationships continues to be nuanced as more light in being shed on the issue.

40 YEARS OF EXPERIENCE WITH THE GERMAN IVF REGISTRY (D·I·R)

Klaus Bühler, *Germany*
Former Chairman of the Deutsches IVF-Register

If, when the German IVF Registry (D·I·R) was founded in 1982 by the then 5 IVF centres, the focus was on demonstrating to a broad public that nothing immoral or unethical was taking place in the centres, the idea of quality assurance and further training was added at the latest after the fundamental reform and conversion to complete electronic data collection in 1997. The D·I·R is supported and financed by the centres themselves. A report is published annually - since 2009 also in English: www.kup.at/D.I.R annuals - in which all results are summarised and anonymised. However, each centre receives a "centre profile" for self-critical review of its own results, in which the individual position is shown in percentile curves for the most important parameters. By this the D·I·R also has an effect on the centres and prompts them to improve their working methods. In the case of particularly conspicuous figures, the Executive Board can lift the promised anonymity and contact the centre concerned directly. The cPR in 2019 after 110,786 treatment cycles was 32.7% and BR was 23.3% with 96.1% of complete records. One of the main goals was and is to reduce the high number of embryos transferred per ET, which is also due to the legal situation in Germany. From 1997 to 2020, the average number could be reduced from 2.56 to 1.69 (fresh/ 2.34 → 1.54 thaw cycle), but it is still too high. Thus, the rates of multiple births at 17% and of 29% in the number of multiple children born are also still far too high, even though since 1997 the rate of triplets born has been reduced by > 85%. Multiples cause >90% of premature births. The D·I·R also wants to show ways out of this dilemma. With the liberal interpretation of the very restrictive Embryo Protection Act since the early 2000s, there has been a steady increase in blastocyst culture. Likewise, the rate of frozen oocytes and embryos also increased. This means that today the cum CPR after ≥4 ET cycles can be reported at 70%, and in women <35y even at 81%. Even with only one OPU cycle, 2/3 of women will be pregnant after ≥4 further thawing ET-cycles. Today, the D·I·R is not only the oldest national IVF registry in the world, but also the largest, with more than 2 million cycles recorded - 90% of the 2 million electronically collected cycles were also recorded prospectively. Prospectivity means that the cycle was registered in the system within the first week after the start of stimulation or 5 days after

thawing, i.e. before the out-come is foreseeable. D·I·R is the only registry that reports a prospectivity rate of the data collected. This makes the data particularly valid.

ORGANOIDS CAN BE ESTABLISHED RELIABLY FROM CRYOPRESERVED BIOPSY CATHETER-DERIVED ENDOMETRIAL TISSUE OF INFERTILE WOMEN
Bich Ngoc Bui, *Netherlands*

Problem statement: Research into the role of the endometrium in infertility has long been hampered owing to limited tissue
availability in laboratories and lack of access to clinical biopsies. Recently, organoids were developed from human endometrium. Organoids are three-dimensional in-vitro structures that recapitulate the original organ's key biological properties and are robustly expandable, thereby offering the possibility to mimic disease- and patient-specific phenotypes. They may provide a valuable tool to perform more in-depth studies into the role of the endometrium in various unexplained reproductive disease states. The use of freshly obtained tissue limits organoid-based research to clinics with organoid laboratories nearby, and it was thus far unknown whether cryopreservation of endometrial tissue affects organoid development and characteristics. If organoid development from cryopreserved endometrial tissue is found reliable, it will allow protocols to be established using banked tissues. The aims of the study were to investigate whether organoids could be established from endometrial tissue of infertile women and whether tissue cryopreservation allows for establishment of organoids comparable to organoids derived from freshly biopsied endometrial tissue. ***Methods:*** Endometrial tissue was obtained from six infertile women through minimally invasive biopsy using a Pipelle catheter and subjected to organoid development, immediately after biopsy as well as after tissue cryopreservation. Organoid formation efficiency, morphology, expandability potential, endometrial marker expression (immunostaining and reverse transcription quantitative real-time polymerase chain reaction) and hormonal responsiveness (after oestradiol and progesterone treatment) were assessed. ***Results:*** Organoids established from both fresh and frozen tissue at comparable efficiency, could be passaged long-term and showed similar morphology, i.e. cystic with a central lumen lined by a single epithelial cell layer. They also exhibited comparable expression of endometrial markers and proliferative activity (Ki67 expression). Finally, organoids from freshly biopsied and cryopreserved endometrial tissue showed similar responses to oestradiol and progesterone treatment. ***Conclusion:*** Organoids can be established from cryopreserved endometrial tissue of infertile women and cryopreservation of the biopsy does not affect organoid formation and overall organoid characteristics.Cryopreservation of biopsies for later organoid development facilitates sample collection from any fertility clinic, not just the ones near an organoid laboratory.

ULTRASOUND SCREENING IN FIRST TRIMESTER @ 11-14 WEEKS
R. Chaoui
Fetal Diagnosis and Human Genetics Center-Berlin-Friedrichstrasse 147, 10117-Berlin

In the early 1990ies a new ultrasound screening policy was introduced by Kypros Nicolaides as a first trimester screening between 11-14 weeks of gestation for the measurement of the fluid behind the neck, called nuchal translucency (NT). The NT screening was completed by biochemistry values from maternal serum to achieve a risk assessment for the presence of common aneuploidies as trisomy 21, 18 and 13. In the last decade however there was an increased uptake of the new cell-free DNA screening for aneuploidy in maternal blood with a high sensitivity and specifity. With the advent of high-resolution transducers in the past two decades, the first trimester NT ultrasound examination has evolved beyond aneuploidy screening and now includes an evaluation of fetal anatomy in early gestation. International and local released guidelines reflect this development. In addition, the measurement of Doppler of the uterine arteries allows along with biochemistry values to assess the risk for preeclampsia. The presentation will focus mainly on the NT screening, the diagnosis of obvious findings in the first trimester and the role of a protocol in the systematic evaluation of the fetus to diagnose anomalies of the CNS, the heart and other organs. First trimester screening should no longer be considered as a solely aneuploidy screening but has evolved to be a screening tool for complex anomalies between 11 and 14 weeks of gestation. However, there is new development toward scanning even before 11 weeks of gestation to detect severe lethal anomalies, followed by a scan at 13 weeks. This however should be followed by a second trimester screening, as some anomalies evolve and some develop between the first and second trimester.

BIOLOGICAL SENSORS OF IN-UTERO MONITORING
Ying Cheong
Medical Director, Complete Fertility Centre; Professor in Reproductive Medicine, University of Southampton; Complete Fertility Centre Ltd, UK

Despite advances in ART, implantation and pregnancy rates per embryo transfer still remain low. IVF laboratories strive to ensure that the process of handling gametes in vitro closely mimics the in vivo environment. The successful adoption of time-lapse incubator technology world-wide suggests that clinicians and scientists place significant emphasis on trying to maintain a stable environment for the developing embryo. However, the data on the key biophysical parameters on oxygen concentration, pH and temperature within the uterus is largely unknown, and often only evaluated in snap-shots. In this talk, I will explain how we have and are currently interrogating the uterine biophysical environment. I will show data on pO2 within the female reproductive tract with cyclical variation and minute-to-minute oscillations, and suggest pathophysiological factors that may influence these parameters. Fine balanced control of pO2 and avoidance of overwhelming oxidative stress is crucial for embryogenesis and implantation. The pH in the female reproductive tract is graduated, with lowest pH in the vagina (~pH 4.42) increasing toward the Fallopian tubes (FTs) (~pH 7.94), reflecting variation in the site-specific microbiome and acid–base buffering at the tissue/cellular level. The temperature variation in humans is cyclical by day and month. In humans, it is biphasic, increasing in the luteal phase; with the caudal region of the oviduct 1–2 degrees cooler than the cranial portion. Temperature variation is influenced by hormones, density of pelvic/uterine vascular beds and effectiveness of heat exchange locally, crucial for sperm motility and embryo development. The notion of ‘back to nature’ in assisted conception suggested 20 years ago has yet to be translated into clinical practice. This talk will highlight our current inability to assess the in vivo reproductive tract environment in real time and introduce future development of sensing technology in utero that may help to provide new insights into how best to optimize the in vitro embryo environment and allow for more precise and personalized fertility treatment.

SYNTHETIC HUMAN ENTITIES WITH EMBRYO-LIKE FEATURES
Susana M. Chuva de Sousa Lopes, *Netherlands*

Human pluripotent stem cells are being used to model different aspects of human development from induced directed differentiation to understand the formation of specific organs (in organoids), to study aspects of human gastrulation, such as axis elongation and symmetry breaking (in gastruloids) and more recently blastocyst formation (in blastoids). In particular the formation of human blastoids have sparked worldwide controversy, as these embryo-like structures, formed by donor-specific human stem cells, may acquire in culture developmental potential to form a complete organism. This developmental potential is however not possible to investigate in humans in vivo for obvious ethical reasons, but also not in vitro due to the lack of suitable developmental models to mimic peri-implantation even considering the current 14-day limit. Moreover, if human pluripotent stem cells prove to be actually totipotent (instead of pluripotent) this would have significant implications regarding the definition of “embryo”. In contrast to human (natural) embryos, the generation and culture of embryo-like structures is not explicitly regulated. This field of scientific research is moving forward very fast and I will review some of the relevant scientific developments as well as touch on potential ethical and legal implications.

BREAST CANCER IN SPECIAL POPULATIONS
Herjan J.T. Coelingh Bennink, *Pantarhei Oncology, The Netherlands*

Problem statement: What is the incidence of breast cancer (BC) in rare but well-defined human populations with major deviations of genetic, sexual, and gender-related structures and functions. ***Methods:*** We have searched the literature for information on the risk of BC in relation to gender, breast development, and gonadal function in the following 8 populations: 1) females with the Turner syndrome (45, XO); 2) females and males with congenital hypogonadotropic hypogonadism and the Kallmann syndrome; 3) pure gonadal dysgenesis (PGD) in genotypic and phenotypic females and genotypic males (Swyer syndrome); 4) males with the Klinefelter syndrome (47, XXY); 5) male-to-female transgender individuals; 6) female-to-male transgender individuals; 7) genotypic males, but phenotypic females with the complete androgen insensitivity syndrome, and 8) females with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome (müllerian agenesis). ***Results and Conclusions:*** Based on this search, we have drawn 3 major conclusions. (i) First, the presence of a Y chromosome protects against the development of BC, even when female-size breasts and female-level estrogens are present. (ii) Second, without menstrual cycles, BC hardly occurs with an incidence comparable to males. There is a strong correlation between the lifetime number of menstrual cycles and the risk of BC. In our populations the BC risk in genetic females not exposed to progesterone (P4) is very low and comparable to males. (iii) Third, BC has been reported only once in genetic females with MRKH syndrome who have normal breasts and ovulating ovaries with normal levels of estrogens and P4. Based on the results of this literature study, we hypothesize that the oncogenic glycoprotein WNT family member 4 is the link between the genetic cause of MRKH and the absence of BC women with MRKH syndrome.

FERTILITY, PREGNANCY AND PERINATAL OUTCOME AMONG PARENTS IN THE FOURTH AND FIFTH DECADE OF LIVE. PRO AND CONTRA
Christian Dadak, *Med University Vienna, Austria*

What means advanced age? There is no exact definition of older age. In earlier time it was 35, today perhaps 40, very old >45,>48 or>50 a. Postmenopausal >55a, „geriatic“ >60a. Mean maternal age for Primipara has changed in the last 30 years from 24 to 29,5. Reasons for this development are longer education, first career, later wedding , contraception, no partner, partner does not want children, perhaps he has already children. The problems in these patients are the increase of chronic diseases and genetic problems. Patients, who prolong pregnancy to a higher age have more problems with fertility,too. The rates of success of ART decreas. Older fathers have also the risk of genetic problems (more Down Syndrom), the impact of older age of fathers on pregnancy is discussed varying in literature.The positive effect of older parents is that children are more often born in a perfectly prepared world.

GENETIC ARCHITECTURE OF REPRODUCTIVE AGEING
Felix Day, *UK*

Reproductive longevity is critical for fertility and plays an important role in the healthy ageing of women. With timing of menopause likely to become of greater importance as larger numbers opt to delay parenthood. Large-scale genetic studies have successfully identified genetic loci with a range of phenotypes in humans and can provide evidence of important biological processes and insights relevant to human health at the population level. The size of these genome-wide studies has been increasing in recent years, and there has been a commensurate increase in the number of loci identified. In total 290 genetic loci have been robustly associated with ovarian ageing, assessed using normal variation in age at natural menopause; and 389 independent signals have been found for age at menarche. These variants explain ~10.1% and ~7.4% of the population variance in these traits respectively. As well as being robustly associated with normal variation in age at menopause, the common alleles, in aggregate, were also associated with incidence of clinical extremes. The genome-wide approach can also help to identify biological processes that underly reproductive aging. In particular, loci associated with menopause implicate a broad range of DNA damage response processes and include loss-of-function variants in key genes involved in these pathways. The importance of DNA damage response was also demonstrated by the association of a common coding variant in BRCA1, the first time that variation at this gene had been associated with any complex trait in these sorts of studies. It has been possible to demonstrate some of these processes in mouse models, highlighting the hypothesis generating nature of these large-scale genetic studies. The work on menarche has reinforced the idea of the importance of neurological control of puberty timing, as well as the existence of a substantial overlap between the genetics involved in adiposity and the start of the reproductive lifespan. Large-scale genetic studies such as these can also provide the basis of causal inference analyses, using Mendelian randomisation methods. These approaches have indicated that extending the reproductive lifespan in women would improve bone health and metabolic health but might also be associated with increases in the risk of hormone-sensitive cancers. This last association is thought to be driven by pathways separate from those related to DNA damage response. When using Mendelian randomisation to consider associations with age at menarche, it is important to account for the substantial overlap of the signals between puberty timing and body mass index. In models that do account for this, it has been shown that changes in puberty timing are associated with breast and endometrial cancers in women and prostate cancer in men. These findings provide insight into the mechanisms that govern reproductive ageing, how they might be targeted by therapeutic approaches to extend

fertility and links to diseases in later life, particularly reproductive cancers.

SHOULD OBESE WOMEN BE ADVISED TO LOSE WEIGHT IN PREGNANCY? NO.
Joachim W. Dudenhausen, *Germany*

Obese mothers are an important problem in obstetrics globally. Advanced maternal BMI complicate pregnancy, gestational diabetes and delivery. It must pointed out that the consequences do not end with delivery, but represent a livelong burden to the mother and the child. Therefore strategies to reduce the BMI of obese women are mandatory, the prevention of complication in pregnancy is important before pregnancy, anteconceptional strategies like physical activities and nutrition adjustment are options to avoid obese pregnant women and the complication.

FREEZE ALL IN ART: TO BE OR NOT TO BE?
Human M. Fatemi, MD, PhD, *ART Fertility Clinics, UAE , Muscat, India*

In recent years the number of frozen-thawed embryo transfer (FET) cycles performed has increased significantly, facilitated by improved laboratory techniques and the increased use of PGT-A in ART. High impact factor published papers on that topic failed to demonstrate any benefit of frozen embryo transfer as compared to fresh embryo transfer. Unfortunately, most, if not all of those studies, do have significant faults, neglecting completely the basic Physiology and the so-called window of implantation. It is well accepted that endometrial morphology changes under the influence of ovarian sex steroids during the menstrual cycle. Endometrial receptivity is driven by the secretory transformation of the endometrium under the influence of progesterone after preceding estrogen exposure. As far back as 1937 the effects of progesterone and estrogen on the endometrium was assessed. Rock and Bartlett reported that it may be possible to determine both the duration of progesterone secretion and the estrogen-progesterone balance from the presence or absence of sequential changes in the endometrium. Subsequently in 1949 a paper was published identifying endometrial histology as the most accurate method of diagnosing corpus luteal insufficiency and established the criterion of a lag in endometrial histology of 2 or more days between expected and observed findings in at least two cycles. In 1950 Noyes et al., documented the daily histological changes occurring under the influence of progesterone and concluded that endometrial dating gives an estimate of quantitative progesterone effect which reflected both duration and amount of progesterone secretion. The histological changes described by Noyes et al in 1950s, has been revalidated recent gene expression models. Hence, ALL stimulated cycles do have an endometrial advancement, due to progesterone rise within 1 hour post final oocyte maturation. This is leading to endometrial advancement and an asynchrony between endometrium and the developing embryo. The Synchrony of the endometrium and the embryo developmental stage is crucial for a correct implantation. As endometrial receptivity is closely correlated to the hours of progesterone exposure following sufficient exposure to estrogen, timing of the embryo transfer is the key step towards a successful outcome in addition to embryo euploidy and embryo quality. Shapiro et al clearly demonstrated that the implantation rate in fresh cycles is directly related to the embryo division pattern and length of progesterone exposure, however, this is not true in frozen cycles. This clearly demonstrated that the fresh cycles are reducing the chance for many embryos to implant by reducing the window of implantation, due to longer exposure of progesterone. Prior conducting a study to compare fresh versus frozen cycles in ART, one has to understand and respect the above-mentioned basic knowledge on physiology. Unfortunately, there is a lack of correctly conducted RCTs to answer the question on what cycle regimen is the best regimen for a frozen embryo transfer and as long as this question in not fully and correctly answered, one can impossibly compare a fresh with a frozen cycle and publish misleading meta-analysis on the topic. Future correctly conducted RCTs are urgently needed to answer this important question.

DUO-STIM ADVANTAGES AND DISADVANTAGES: CON
Bart Fauser, *MD, PhD, FRCOG, Prof.Em. of Reproductive Medicine, University of Utrecht, The Netherlands*

The approach of duo-stim essentially refers to ovarian stimulation for IVF in the luteal phase next to follicular phase stimulation. Hence, ovarian stimulation twice during a single ‘menstrual cycle’. However, a ‘cycle’ no longer exists when ovaries are stimulated for multiple follicle development and multiple oocytes being subsequently retrieved for fertilization in vitro. Ovarian physiology teaches us that follicles are ready to be stimulated to ongoing and gonadotropin dependent growth any time during the menstrual cycle. Early follicle development is a continues process which takes place independent from support by gonadotropins. Only at a later early antral stage of development, follicles will continue its development when FSH serum concentration surpass a certain threshold (also referred a secondary recruitment). Indeed, various clinical studies have shown that the concept works. The advantages of stimulating follicle development with continued (or duo or tri, if you wish) stimulation are clear. In case of the need to undergo gonadotoxic treatments it is wise to harvest multiple oocytes as soon as possible allowing for optimal fertility potential at a later stage. However, the optimal way to achieve this goal in terms of stimulation protocols have not been carefully studied.

ULTRASOUND IN THE DELIVERY ROOM
Tullio Ghi, *Italy*

The assessment and management of a woman in labor is traditionally based upon clinical examination. The diagnosis of labor arrest and the timing of interventions rely on the digital evaluation of cervical dilatation and effacement, fetal head station and position. However, clinical examinations of station and position are inaccurate and subjective, especially when a caput succedaneum impairs palpation of the sutures and fontanels. The use of ultrasound has been proposed as an aid in the management of labor. Several studies have demonstrated that ultrasound examinations are more accurate and reproducible than clinical examinations in the diagnosis of fetal head position and station and in the prediction of labor arrest. Ultrasound examination in labor can to some extent, predict which laboring women in the second stage are destined for spontaneous vaginal delivery or operative delivery. Finally, there is growing evidence that US in labor may predict the outcome of instrumental vaginal delivery. Ultrasound in labor can be done transabdominally, mainly for head position and spine position or transperineally (TP) for assessment of head station and position at low stations. Several quantitative sonographic parameters have been proposed to assess head station. Recently the guidelines on the appropriate use of labor ultrasound have been published by the International Society of Ultrasound in Obstetrics and Gynecology. In this document it is recommended when ultrasound should be performed in labor, which parameter(s) should be obtained and how the sonographic findings should be integrated in the clinical practice in order to improve the management of the patient.

DEBATE: STIMULATION: WE SHOULD NOT USE MORE THAN 150 UNITS IN MOST PATIENTS - CON
Norbert Gleicher, *USA*

The concept of mild stimulation can be viewed as one among many so-called “add-ons” to IVF, responsible for declining pregnancy and live birth rates all over the world. We in this debate will argue that mild ovarian stimulation for everybody has no evidentiary basis but, even more importantly, has no basic logical basis in biology.

WHY THE PGT-A HYPOTHESIS FOR BIOLOGICAL REASONS, SIMPLY, CANNOT WORK
Norbert Gleicher, *USA*

PGT-A, before given the acronym PGS, involves embryo biopsy prior to transfer under the original hypothesis that elimination of aneuploid embryos prior to transfer will improve implantation, pregnancy and lie birth rates of remaining embryos and reduce miscarriage rates. We will here demonstrate why the hypothesis because of basic biological observations affecting preimplantation-stage embryos simply cannot work.

THE HYPO-ANDROGENIC PCOS-LIKE PHENOTYPE AT ADVANCED AGES, ONE OF THE MOST FREQUENT CAUSES OF REPEAT IVF FAILURE
Norbert Gleicher, *USA*

As a “syndrome.” PCOS is an amalgam of 4 s-called phenotypes (A, B C and D), all but D under Rotterdam criteria considered hyper-androgenic. We here will propose that phenotype-D, like all other phenotypes at young ages (< 25years) is hyperandrogenic, then due to declines in adrenal androgen production for ca. 10 years goes through a normo-androgenic phase (the reason why this phenotype is widely seen as normo-androgenic) and, ultimately, after age 35 becomes increasingly hypo-androgenic, therefore give the acronym hyper-hypo-androgenic PCOS (HH-PCOS). Because of this hypo-androgenism, it becomes treatment resistant, unless testosterone levels are restituted. Because women with D-phenotype are lean and do not have “classical” stigmata, they often go undiagnosed.

IS PERIPARTUM CARDIOMYOPATHY AN AUTOIMMUNE DISEASE?
Norbert Gleicher, *USA*

We in this presentation will offer evidence for why PPCM for several convincing reasons should be considered an autoimmune disease.

CHROMOSOME ERRORS IN HUMAN EGGS SHAPE NATURAL FERTILITY
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Chromosome errors, or aneuploidy, affect an exceptionally high number of human conceptions and lead to congenital disorders or pregnancy loss. In our study, we followed chromosome segregation patterns directly in human oocytes from females spanning a majority of the reproductive age spectrum, 9 to 43 years. We found that the rate of abnormalities in oocytes follows a U-shaped curve, suggesting that aneuploidies at both young and advanced ages are female in origin. Unexpectedly, specific segregation errors showed different age-dependencies, therefore providing a quantitative explanation for the U shape. Increased aneuploidy in young girls and women (<20) was preferentially associated with whole-chromosome nondisjunction (MI NDJ) events. Whereas women of advancing age (≥33) showed centromeric or more extensive cohesion loss through premature separation of sister chromatids (PSSC) and reverse segregation (RS) events, respectively. This centromeric or more extreme cohesion weakening may be acting as a “molecular clock” to limit pregnancies as women age by introducing specific chromosomal errors, without causing genome-wide missegregation. A second, and currently unknown, mechanism could then account for the high MI NDJ rates seen in young females. Together, these two mechanisms create a chromosome-based system that forms the U-curve of aneuploidy in oocytes, thereby shaping the distinct natural fertility curve in humans.

THE ROLE OF SECONDARY PREVENTION IN CMV-VALACICLOVIR, HYPERIMMUNE IMMUNOGLOBULINS
Max Hackelöer, *Germany*
***Introduction*:** Congenital cytomegalovirus (CMV) infection is the leading cause of non-genetic deafness, mental retardation and neurological deficits in children worldwide. Congenital infection is based on primary CMV infection, reactivation of an existing infection or reinfection during pregnancy. In the case of a primary infection during pregnancy, the probability of materno-fetal transmission is about 40%. In case of reactivation/re-infection, the intrauterine transmission rate is estimated to be 0.5-1.2%. The prevalence of congenital CMV infection varies between 0.6 and 6.1% in developing countries. As there is no general CMV screening in pregnant women or newborns in Germany, precise data on prevalence in Germany are lacking. Approximately 11% of congenitally infected infants show symptoms at birth. These children have a 30 – 40% risk of long-term sequelae including sensorineural hearing loss, developmental delay, psychomotor impairment and cerebral palsy. The risk for a symptomatic neonate is highest if maternal seroconversion occurs in the first trimester. With increasing duration of pregnancy, the

transmission rate increases whereas the rate of symptomatic infants decreases. Two main treatment options are available to prevent materno-fetal transmission: Hyperimmunoglobulins (HIG) and Valaciclovir. After fetal infection, therapeutic options are limited.

Hyperimmunglobulins (HIG): In the past, numerous studies examined the efficacy of HIG to prevent materno-fetal transmission. Several studies came to partly contradictory results. In a 2005 non-randomized study by Nigro et al., pregnant women in the HIG group received 2-7 HIG doses at 100 IU/kg body weight (bw) at 4-week intervals. A significant (p = 0.02) reduction in transmission was demonstrated in the HIG group (n = 37) with six CMV-positive infants (16%) compared to the control group (n = 47) with 19 CMV-positive infants (40%). Furthermore, there were no increased pregnancy complications in the HIG group, so that the application was classified as safe. In the first prospective randomized controlled trial of HIG therapy in pregnancy conducted by Revello et al. in 2014, the results of Nigro et al. were not confirmed. Pregnant women in the HIG group received a dose of 100 IU/kg bw at 4-week intervals, analogous to the procedure of Nigro et al. In the HIG group (n = 61) 18 children (30%) and in the control group (n = 62) 27 children (44%) were infected at birth (p = 0.13). Furthermore, in contrast to Nigro et al., the HIG group tended to have a higher incidence of pregnancy complications. For example, more preterm births were recorded in the HIG group (7/48; 15%) compared to the control group (1/47; 2%). In 2021, Hughes et al. published the analysis of the second randomized placebo-controlled double-blind trial to date with 399 pregnant women from the USA. Pregnant women in the HIG group received 100 IU/kg bw of HIG intravenously every month until delivery. After the interim analysis, the study was stopped because no significant difference was detected, with transmission rates of 22.7% (46/206) in the HIG group and 19.4% (37/193) in the control group. The rate of preterm birth was comparable in both groups (12.2% vs. 8.3%). The amount of HIG administered and the time interval between administrations were similar in all studies listed above and were based on an assumed CMV IgG antibody half-life in maternal blood of about 22 days. More recent studies show a much shorter half-life of antibodies in blood of approximately 11 days. A recent study by Kagan et al. investigated the transmission rate in pregnant women with a primary CMV infection in the first trimester. In contrast to the previously described studies, the subjects in the HIG group received antibodies at fortnightly intervals at a higher dose of 200 IU/kg bw until 20 weeks' gestation. In the HIG group (n = 40), the three infants infected with CMV at birth (7.5%) were asymptomatic. In the historical comparison cohort (n = 108), 38 children (35.2%) were affected. Thus, the transmission rate after HIG prophylaxis was significantly reduced from 35.2% to 7.5% (p = 0.001). The incidence of pregnancy complications, especially preterm births, was comparable in both groups. A retrospective data analysis of pregnant women who received HIG with the aim of transmission prophylaxis at the Charité - Universitätsmedizin Berlin between 2010 and 2017 yielded similar results. Analogous to Kagan et al., a dose of 200 IU/kg was used at fortnightly intervals. In contrast to Kagan et al., inclusion was up to the second trimester. The first HIG treatment took place at a mean of 17 SSW. Nevertheless, a significantly lower (p=0.026) transmission rate of 23.9% was observed in the HIG group (n=46) compared to the historical cohort (n=281) with a transmission rate of 39.9%. **Valaciclovir:** Since data on the efficacy of HIG to prevent materno-fetal transmission are heterogenous, more recent studies investigated the efficacy of antiviral therapy. Medications such as aciclovir and valaciclovir are considered safe in pregnancy and have been commonly used to treat herpes simplex infections or pregnant with CMV-primary infection and confirmed transmission. A French study showed good placental transfer and that valaciclovir was well tolerated with rare adverse events in pregnant women. In 2020, Shahar-Nissan et al. published the results of a randomized, double-blind, placebo-controlled trial looking at 90 women with a primary infection in the first trimester or periconceptional period. The women were divided into a treatment group (n=45) receiving 8g valaciclovir every day until amniocentesis and a placebo group (n=45). Shahar-Nissan et al. were able to show a significant decrease of the transmission rate from 29% in the group without treatment to 11% in the valaciclovir group. The benefit of valaciclovir in secondary prevention was confirmed in the study of Faure-Bardon et al. who were able to show a reduction in fetal infection in the treatment group with an odds ratio of 0.318 (95% CI, 0.120–0.841); P=0.021). ***Conclusion*:** Studies on the efficacy of HIG are heterogeneous. An early start of therapy in the first trimester and a sufficiently high dose at two-week intervals seem to be decisive for the success of therapy. The current amount of data on HIG is not sufficient for a general recommendation in national and/or international guidelines. Recent studies confirmed the acceptability, tolerance and benefit of secondary prevention by valaciclovir. Key to success with this treatment regime seems to be a well-established routine maternal serum screening policy in the first trimester of pregnancy.

STANDARD IVF VS ADD-ON IVF – FUTILE EXPENSE? WHAT IF THE PATIENT IS WILLING TO PAY FOR ADD-ONS?

Joyce Harper, *EGA Institute for Women's Health, University College London, UK*

IVF add-ons are additional treatments which are not essential for an IVF/ICSI cycle but often claim to improve live birth rate (LBR). To make a claim that a treatment improves LBR, ideally there should be evidence from one or more high quality randomised controlled trials (RCT). In the UK, the Human Fertilisation and Embryology Authority (HFEA) has designed a traffic light system to rate add-ons which is presented on a patient facing web site. A red rating means there is no evidence to show that the add-on will improve LBR, amber means there is conflicting evidence and green means there is robust evidence. Currently, none of the add-ons on the HFEA web site are rated green. Add-ons have been the subject of much debate as they are frequently used, with a high financial cost to the patient. Recently the Competition and Markets Authority and the HFEA have worked together to produce recommendations on the use and advertising of add-ons in the UK. A newly formed ESHRE working group is investigating IVF add-ons.

IS VAGINAL LASER AN EFFECTIVE TREATMENT OF STRESS URINARY INCONTINENCE?

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Stress Urinary Incontinence is a common and debilitating problem that can affect women at all ages but is particularly common around the time of the menopause and early post-reproductive years. The underlying cause is usually weakness of the urethral sphincter mechanism and surrounding pelvic floor musculature which is often secondary to pregnancy and childbirth and exacerbated by age and menopause related changes. However, there are other potential causes that need to be excluded before any treatment is commenced and accurate clinical assessment of the problem by an appropriately trained health professional is required. Conservative therapy, which includes appropriate life style advice and a full course of pelvic floor physiotherapy, should always be the first line of management in women with SUI. The aim of vaginal laser therapy for SUI is to strengthen the connective tissue of the sub-urethral hammock and surrounding supporting fascia. To date there have been around 20 publications assessing

the efficacy of vaginal lasers in SUI, predominantly with the Erbium Yag. The majority are small prospective observational studies or case series with follow up of 3-6 months and only a handful have had a follow up of 12 months or more. Outcome measures are largely subjective using questionnaires. Overall, there appears to be a modest improvement in symptom scores for around 6-12 months with a gradual return to baseline after that unless repeated treatments are undertaken. Women with mild USI seem to do best.It would be premature to draw any conclusions about the clinical usefulness of laser for SUI from these data. Only a few of the studies have used any objective outcome measures (e.g. urodynamics or pad test) which is the recognised standard for the evaluation of other SUI interventions. It is unclear what conservative therapy most of these women have been offered prior to laser treatment. Any minimally invasive intervention for SUI should only be considered after an unsuccessful course of pelvic floor muscle training (PFMT). Thereafter randomised trials against other standard minimally invasive interventions such as bladder neck bulking agents or electrical stimulation are required to help gauge the usefulness and likely role of this modality in the management of USI. Whilst the vaginal laser generally seems well tolerated with small numbers of adverse events, it is not a procedure without some risk. It is beholden on all of us to ensure we do not start advocating widespread adoption of new techniques such as this until they have been fully evaluated both in terms of their efficacy and safety. Those performing these procedures should do so in the context of research with appropriate governance and transparency.

SOME HISTORICAL AND GENERAL CONSIDERATIONS ON NIPT- GREAT PROGRESS ACHIEVED, BUT WE HAVE TO PROCEED WITH CAUTION

Wolfgang Holzgreve, *Professor of Obstetrics and Gynecology, Medical Director and CEO of the University Hospital Bonn, Germany*

Ever since we have recordings in history of human thoughts and emotions there is evidence for concern of expectant parents regarding the health of their unborn child. In the past, however, the ability to find out whether the growing fetus had problems in its development was very limited. Especially in the 70s this changed with the introduction of diagnostic ultrasound which allowed to visualize the features of the unborn child without harm, and around the same time biochemical marker screening approaches were developed for the prediction of neural tube defects or chromosomal anomalies in the fetus. The improvements of the ultrasound technology quickly allowed amniocentesis to be performed around 16 weeks of pregnancy and since the middle of the 80s chorionic villus biopsy at around 10 weeks of gestation. Ultrasound will most likely never be fully replaced in pregnancy surveillance by genetric techniques, because the majority of the structural defects to be detected prenatally which constitute the majority of the 2-4 % congenital anomalies, are multifactorial (e.g. cardiac or neural tube defects) but the new powerful screening tests have to be combined in a logical and affordable way. In the meantime fetal Rhesus D antigen genotyping in D-negative mothers is one of the many positive examples of applying Non-invasive Prenatal Testing in clinical practice. The traditional approach of administring anti D immmunoglobuline to all D-negative mothers is needless in the 40 % of pregnancies with a D-negative fetus.Since the 70s there was an intense search for a non-invasive method of prenatal diagnosis, and in a collective effort of international research first the isolation of fetal cells from the blood of pregnant women was tried whereas later this method became successful and clinically mature by looking at cell-free DNA in the maternal blood. Because progress in medicine through publications, lectures and media travels fast these days, now more than 10 million cases have been investigated noninvasively by the NIPT methodology. In ethical terms, Non-invasive Prenatal Testing (NIPT) is a major breakthrough and progress for the women concerned and even helps to understand better pregnancy-related diseases such as preclampsia and autoimmune diseases.The introduction of NIPT is a positive example for how a new technology should be introduced into clinical practice, that is after the research and development after careful planning the proper trials were performed. So that the public was prevented from an immature technical approach spreading into clinical use without rigorous evaluation. Apart from the prenatal diagnosis of trisomies the detection of fetal sequence variants in cffDNA not present in the mother is now reliably feasible by a variety of techniques such as RTQ-PCR, digital PCR and more recently HTS and applicable for a number indications such as paternally inherited dominant conditions or autosomal recessive conditions with different mutations in both parents as well as new mutations. NIPT in addition to being a reliable method for the prenatal detection of chromosomal anomalies, microdeletions is becoming a valid option for a growing number of monogenic conditions. Some of the approaches are rather complex, however, and it remains to be seen what parents and health care systems with an insurance based solidarity principle are ready to invest in order to avoid the risk of an invasive procedure allowing simple and accurate testing. Our genetic counselling, which has the aim of allowing women to make their own decision based on proper and up to date information, constantly has to be updated based on the progress in this dynamic field of medicine. The so-called “Information consent” has to be thrieved for, but it is always a challenge for counsellors to make sure that counselees can understand the complex information and statistics and can ultimately make decisions in accordance with their own beliefs and judgement.

PCOS: A BRAIN DISEASE?

Joop S.E. Laven, *Erasmus University Medical Center, Rotterdam, The Netherlands*

Polycystic ovary syndrome (PCOS) is an endocrine condition associated with reproductive and psychiatric disorders, and with obesity. Eating disorders, such as bulimia and recurrent dieting, are also linked to PCOS. Moreover it seems that there is a profound dysregulation of the HPG axis causing the ovarian phenotype. PCOS is also highly associated with psychological distress and body dissatisfaction. Finally it also associated with eating disorders and disordered eating. The brain disorder hypothesis is based on events that occur during a largely neglected stage of female reproductive development e.g. intra uterine life. To date, most research into the origins of PCOS has focused on the prenatal induction of this disorder, particularly in utero androgenization and the role of anti-Müllerian hormone (AMH). Moreover, it seems that the wiring of the midbrain and the hypothalamus is different in offspring of rats that were prenatally overexposed to AMH leading to an overactive HPG axis as well as to the psychological stressors and disordered which eventually establishes the PCOS phenotype. Since the initial changes seem to occur in the brain PCOS is a brain disease with an ovarian phenotype as well.

THE MICROBIOME -DOES IT REALLY MATTER TO ART?

Joop S.E. Laven, *Erasmus University Medical Center, Rotterdam, The Netherlands*

The existence of an extensive microbiome in and on the human body has increasingly dominated the scientific literature during the last decade. A shift from culture-dependent to culture-independent identification of microbes has occurred since the emergence of next-generation

sequencing (NGS) techniques, whole genome shotgun and metagenomic sequencing. These sequencing analyses have revealed the presence of a rich diversity of microbes in most exposed surfaces of the human body, such as throughout the reproductive tract.
For the field of reproductive medicine, determination of what is a favorable reproductive tract microbiome provided insight into the mechanisms of both unsuccessful and successful human reproduction. Results of recent studies using different decision strategies as well as different sampling strategies will be presented. To increase pregnancy chances with live birth and to reduce reproduction-related health costs, we have introduced the so called ReceptIVFity® test capable of predicting chances of pregnancy prior to treatment. In case one decides to postpone the treatment based on the test result a considerable increase in pregnancy rates is observed. In case all women would postpone their treatment the absolute increase in pregnancy rates seems to approach 10%. Hence a proper assessment of the vaginal microbiome prior to an ART treatment might further increase success rates of these treatments.

USE OF HRT FOR CARDIOVASCULAR PREVENTION

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Hormonal replacement therapy (HRT), also called menopausal hormone therapy (MHT), is indicated for relief of climacteric symptoms. However, it has also been demonstrated that women might benefit from MHT in terms of prevention of long-term consequences of estrogen-deficiency. Notably, despite the heterogeneity of published studies, a significant reduction of overall mortality has been reported, especially for women who start with long-term MHT early after menopause. This also holds true for the prevention of cardiovascular disease. Noteworthy, climacteric symptoms are associated with an increased risk of hypertension and cardiovascular disease. MHT may prevent chronic conditions like these, especially when started in symptomatic women before the age of 60 years or within 10 years of the onset of the menopause. In addition, individual patient characteristics and risk profiles of each given woman have to be considered. A review about the existing literature is provided.

TESTOSTERONE OR NOT TESTOSTERONE IN MENOPAUSE: THAT'S THE QUESTION!

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There has been much controversy over the last few years as to the precise role of endogenous androgens in women and the place of exogenous androgen replacement in women with distressing low sexual desire. What is not in dispute is that healthy young women produce approximately 100 – 400 mcg per day. This represents three to four times the amount of estrogen produced by the ovaries. Approximately half the endogenous testosterone and precursors are derived from the ovaries and half from the adrenal glands. Testosterone contributes to sexual desire, arousal and orgasm; clearly there are other factors involved including psychosexual, physical, iatrogenic and environmental. The decline in testosterone levels which occurs throughout a woman's lifespan, and particularly so after a surgical menopause when testosterone production decreases by 50% within days of the surgery, has been associated with a number of distressing symptoms (not just sexual) including reduction in well-being, energy levels and mood. Additionally, there appears to be a synergistic effect muscle mass. In view of the important functions of endogenous testosterone it is surprising there has been so little research into the sequelae of deficiency (less than research into conditions of excess androgens such as PCOS). Equally surprising has been the dearth of development of products specifically targeted at female androgen replacement. In the absence of research and development in these areas it is not surprising that many women and healthcare practitioners (HCP) still perceive testosterone as an entirely male hormone and testosterone replacement within the domain of the andrologist. There is also a considerable amount of suspicion that this "male" hormone is worthy of consideration of replacement in women with an apparent deficiency state. There are even accusations that low libido states have been invented by husbands, male physicians, or pharma companies hoping to capitalize on this "pseudo condition" with expensive drugs. The immediate reaction of both patients and practitioners alike is "what are the risks" with concerns of hyperandrogenism with hirsuitism, cardiovascular disease and breast cancer usually top of the list. Concerns regarding side effects and long term adverse events seem to ignore the following fact; genuine testosterone replacement aims to replace deficiency, not to create supra-physiological levels. Women do not develop symptoms and signs of hyperandrogenism if levels are kept within the physiological range. The prospective randomised studies of physiological testosterone replacement which demonstrate a benefit for low libido, do not show an association with cardiovascular or breast disease.[1-2] A recent meta-analysis and a global consensus statement have added to the totality of reassuring data and advice regarding the effectiveness and safety of testosterone usage in women.[3-4] However, the current philosophy of the regulatory authorities with regards to testosterone and the potential for adverse events seems to be that absence of evidence for long term harm is not evidence of absence! What is available to women and their HCPs? Implanted pellets of testosterone are now unlicensed and only available from the USA. Whilst a convenient and highly effective way of replacing testosterone over periods of six months, these pellets tie the patient to her HCP and there is lack of flexibility to change dosage. Intrinsa® testosterone patches were licensed in Europe for the treatment of hypoactive sexual desire disorder (HSDD – distressing low sexual desire) in surgically menopausal women receiving HRT, but the license was withdrawn, largely for commercial reasons, following failure to obtain approval for natural menopause and use without HRT. Other preparations, injectables, patches and gels licensed for male androgen replacement have been prescribed off label by specialists but this leads to confusion of the pharmacist and patient in trying to get the preparation and the dosage right, reducing confidence in usage. Even if therapy is commenced by the specialist, primary care often refuse to continue prescribing, citing cost, lack of familiarity with the product and inexperience in the whole area. The two most commonly used 1% testosterone preparations in women (at 1/10th of the dose) are Testim® tubes and Testogel® sachets. AndroFeme 1® 1% testosterone cream is now licensed for female use in Australia and exported to other countries such as the UK, but only available for private purchase. Compounded bioidentical preparations are not recommended by health authorities or menopause societies. Going forward, investigators, regulators and the pharma industry must collaborate to produce viable androgenic options licensed for female usage. This will ensure that women who would genuinely benefit from this type of replacement are not denied an intervention that could have truly life transforming effects.[2]

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UPDATE ON PRACTICAL PRESCRIBING OF NEW HORMONE THERAPY REGIMENS

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The adverse outcomes seen in The Women's Health Initiative (WHI) combined hormone therapy trial were mainly to an over-dosage of HRT in a relatively elderly population. However, fundemental differences exist between conjugated equine estrogens and 17 beta estradiol and between medroxyprogesterone acetate and other progestogens. It is likely that these differences also contributed to the adverse outcomes in WHI, which were contrary to the cardiovascular benefits seen in previous observational trials. In addition to binding to the progesterone receptor, many progestogenic compounds also bind to the glucocorticoid, mineralocorticoid and androgen receptors. This can lead to unwanted effects such as unfavourable glucose metabolism, fluid retention, acne, weight gain**.** Recent studies of cardiovascular risk markers in younger women have therefore been designed using predominantly 17 beta estradiol and progesterone or dydrogesterone as primary interventions. Menopause societies are now advising that natural progesterone and dydrogesterone may have more favourable cardiometabolic and breast effects compared to synthetic progestogens.[1] Natural progesterone and dydrogesterone do not attenuate the beneficial effects of estradiol in reducing insulin resistance and arterial compliance. There also appear to be differential effects of progesterone and progestogens on breast tissue. Progesterone has a neutral and dydrogesterone a pro-apoptotic effect on breast epithelial cells, whereas androgenic progestogens such as medroxyprogesterone acetate appear to have a proliferative effect, possibly through non-specific effects on the glucocorticoid receptors and gene expression. This might explain the small increase risk in breast cancer promotion in some studies when synthetic progestogens are combined with estrogen. Observational data such as the French E3N cohort and the Finnish registry cohort suggest that women using natural progesterone and dydrogesterone are not at increased risk of breast cancer within the first five years of use; ideally these data will be confirmed in the future by definitive long term, randomised prospective studies. Recent data support the efficacy and safety of lower doses of hormone therapy than previously used. Trials have recently documented the efficacy of 0.5 mg 17β-estradiol combined with either dydrogesterone or norethisterone in treating menopause symptoms. Low dose and ultra-low dose regimens have also been shown to prevent osteoporosis. However a large proportion of clinicians continue to initiate HRT at standard or high doses. This can lead to estrogenic and progestogenic side effects and cessation of therapy. More concerning is the possibility that women are being exposed to an unnecessary risk of some conditions. Data show that higher oral estrogen doses can result in increased risks such as venous thromboembolism and stroke. There may be a dose response effect of estrogen and progestogen for breast cancer risk though this has never been confirmed. At a time that there is concern about the role of progestogen in breast cancer genesis, it behoves us to use the minimum effective dose of progestogen for endometrial transformation. Women who have been through an early menopause or with premature ovarian insufficiency should continue to be treated with higher doses of estrogen as this is more physiological for them.[2] The exceptions to low starting dose should include women with severe osteoporosis and severe psychological symptoms as these women benefit from the dose response effect of higher levels of estrogen. Women who are at risk of venous thromboembolism e.g. obese, diabetic etc should be treated with transdermal estrogen, particularly when higher doses of estrogen are required. Replication of the physiological hormonal environment with estradiol, favourable types of progestogens and progesterone and where required physiological doses of testosterone, can therefore maximise benefits and minimise side effects and risks of HRT. We must also be mindful of the importance of local hormone therapy in women with vulvovaginal atrophy symptoms. It is time we moved away from the notion, often propagated by epidemiologists and the media, that all hormone therapy products have a single class effect, and move towards a more individualised approach to hormone therapy.

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DOES SOCIAL EGG FREEZING INCREASE WOMAN'S EMANCIPATION?

Guido Pennings, *Belgium*

There is much ambiguity about the effect of elective egg freezing (EEF) on the position of women. One line is defending EEF as liberating and increasing reproductive autonomy of women while the opposite line argues that the social context in which women's decisions are made prevents real autonomous decision making. This social context is largely limited to the organisation of the labour market. This reasoning assumes that the reason for postponing childbirth is the incompatibility of work and family/private life. However, all studies show that the primary reason for women to consider elective egg freezing is the lack of a partner. The first question then is where this shortage comes from and how it can be remedied. The main cause of the 'lack of partner' issue for highly-educated women (the group most involved in elective egg freezing) is the reversed gender gap in education. The future is looking bleak for highly-educated women on the partner market as they will largely outnumber university educated men. Obviously, the fact that EEF is not reimbursed in most countries generates a self-selection that makes it difficult to know whether the population would be different if reimbursement would be offered. If EEF would be reimbursed, poorer and lower educated women could theoretically avail themselves of the procedure but they are unlikely to do so because they do not experience a similar shortage of potential partners. Reimbursement would thus lead to a larger uptake in an already privileged group and might actually further increase injustice rather than diminish it. It is concluded that EEF may increase individual reproductive autonomy for some women but does not increase reproductive freedom for the group of highly-educated women. Regardless of how many women would freeze their eggs, a large number of educated women will eventually have to choose between going it alone as a single mother or looking for another life goal. Finally, some policy measures are proposed to reduce the gender gap and thus remove the real cause of the problem. Many authors have looked at the reorganisation of the labour market or at measures to enable women to have their child earlier. Little effort has been put into designing policy changes that tackle the 'lack of partner' issue. One measure could be to introduce special programmes to support men

to start and finish university or tertiary education. If the current trend continues, male students will become a minority and many European countries already have programmes to promote the inflow of minority groups to higher education. This would extend the pool of potential marriage partners and society needs more highly-educated people anyway. Another possibility is to work at more flexible and egalitarian gender roles and to do away with the old breadwinner-homemaker stereotypes. This goal would contribute to many purposes but it would also facilitate women to 'marry down' in terms of education. It is concluded that the main cause of EEF is not female discrimination on the work floor but an unanticipated contingency of the emancipation of women in education. Women's emancipation has increased women's access to education and resulted in a reversed gender gap. This gender gap in education generates a large group of women who hold better positions, earn more money and have a higher education than men. Given the rules of the marriage market, highly educated women will have a hard time finding a partner of the same level.

20 YEARS OF GYNAECOLOGICAL CAPACITY BUILDING IN CAMEROON THROUGH PARTNERSHIP

Patrick Petignant, *Switzerland*

Geneva University Hospitals (HUG) and Health Minister of Cameroon are working together since 1980 in a balanced partnership allowing postgraduate training of Cameroonian doctors in University of Geneva and the possibility for medical students to benefit from internships in Cameroon in tropical medicine. The collaboration between HUG and Cameroonian Health Minister in the field of cervical cancer has been established since 1999 in a project entitled "Promoting Comprehensive Cervical Cancer Prevention and Better Women Health in Medium and Low-Resource Settings" with the aim to develop a cervical cancer screening and prevention adapted to Cameroon. More recently (2014), a collaboration between the HUG and the University of Dschang has been established. University of Dschang is one of the largest institutions of higher education in the West Cameroon which provide an excellent environment for training and research. This partnership is now a highly productive platform of research, which resulted in a large variety of academic activities. Cervical cancer prevention in low-resource setting is a major priority of WHO which consider that the introduction of new technologies may play a crucial role for reducing cervical cancer morbidity and mortality in low-resource setting. Our screening program is in line with the global strategy of WHO and the aim of the presentation will be to present an overview and perspectives of this partnership.

THE IMPACT OF SFLT/PLGF RATIO ON THE PREDICTION AND MANAGEMENT OF PREECLAMPSIA

Luisa Pinto, *Portugal*

The impact of the sFlt/PlGF ratio on the prediction and management of Preeclampsia The incidence of Preeclampsia (PE) is around 2-5% but it still constitutes a major cause of maternal morbidity and mortality. Its origin relies on placental dysfunction, which triggers a decrease in angiogenic and an increase in antiangiogenic regulatory factors. This imbalance is responsible for all the systemic manifestations associated with PE. In most countries the diagnosis of PE still relies on new onset hypertension (HT), associated with proteinuria or clinical or laboratory findings resulting from end organ lesion. This definition has several limitations – it does not allow for a prediction of evolution, appearance of complications or adverse outcomes and it does not differentiate PE from other diseases characterized by HT and proteinuria, which will lead to late recognition of the disease, unnecessary hospitalizations and wrong clinical approaches. The PROGNOSIS study showed that an sFlt/PlGF ratio bellow 38 has a very high negative predictive value in excluding PE in the following week (99,3%) and even in a 4-week period (94,3%). Other studies showed that the sFlt/PlGF ratio is useful for establishing an accurate diagnosis of PE at a cut-off > 85 for early onset PE and > 110 for late onset PE with specificities of 99,5% and 95,5% respectively. Although some studies have shown that different levels and different increases in the sFlt/PlGF ratio correlate with different outcomes, potentially allowing individual risk stratification, no simple or usable formulations came out of these sequential measurements and the putative predicitive ability of different levels of the ratio in women with PE is still difficult to implement in clinical practice. The sFlt/PlGF ratio seems to be useful in diagnosing PE in circumstances in which HT and proteinuria are already present before pregnancy as is the case of chronic renal disease and systemic lupus erythematosus, in which the differential diagnosis between aggravation of underlying disease and PE is even more challenging. We are standing before a new paradigm shift in PE diagnosis and prediction and the integration of angiogenic and antiangiogenic markers in guidelines seems the next logical step to increase diagnostic accuracy and outcome prediction.

FMR1 AND THE GENETIC CONTROL OF FOLLLICULOGENESIS

Julia Rehnitz, *Germany*

During folliculogenesis controlled ovarian follicular maturation is essential and mainly depending on the individual ovarian follicular pool and age. Diminished ovarian reserve (DOR) and premature ovarian insufficiency (POI) are related disorders that impact individual spontaneous pregnancy success rates and success rates during assisted reproductive techniques (ART). Women with DOR are at increased risk of poor ovarian response (POR) during ART. Numerous genes are supposed to play a role in the highly orchestrated network of follicular maturation. The *FMR1* (Fragile X-Mental Retardation 1, OMIM: *309550) gene is located on the X chromosome (Xq27.3). It is supposed to be one of the most prominent folliculogenesis related genes, because of its high mutation frequency and its association with POI. It contains a variable CGG base triplet in its promotor region, that in case of an expansion between 54 and 200 is termed as "premutation" (PM). PM allels in women are associated in 20% with POI and therewith the most common genetic cause of it. It is also called the fragile X POI (FXPOI, OMIM # 311360). The protein FMRP is mainly localized in brain and in the granulosa cells (GCs) of ovarian follicles at different stages and can be a part of an RNA-induced silencing complex (RISC) in the cytoplasm. *FMR1*-PM allele carriers produce elevated mRNA levels, causing reduced FMRP levels due to a negative feedback loop mechanism. *FMR1*/FMRP expression level thus appear to be an important ovarian regulatory mechanism. In our working group we aim the elucidation of several regulatory mechanisms of *FMR1*/FMRP during folliculogenesis and their relation to ovarian disorders. We here present our latest results: We could demonstrate in native GCs of women with poor ovarian reserve, that those with remarkably low CGG repeat lengths also show elevated *FMR1*-levels. So, we assumed here for this genotype an effect on ovarian response. In addition, we discovered novel epigenetic factors, namely CpG methylation patterns in three distinct genomic regions in the *FMR1* promotor region putatively involved in *FMR1* transcription rate and ovarian response in human. Moreover, *FMR1* expression seems to be linked with the mTOR signaling pathway, a known major regulator during early and later folliculogenesis. We found mainly mTOR and S6K linked to *FMR1*. Our results were consistent in human granulosa cells in vitro and in vivo in patients with distinct ovarian

reserve and recently confirmed in blood samples of women suffering from POI.

AUTOMATION IN EMBRYO CULTURE

Laura Rienzi, *Italy*

In the ART laboratory, automation can have different applications: 1) develop new culture systems to improve embryo culture conditions, therefore improving the efficacy of treatments; 2) develop new approaches for embryo selection, hence improving treatments efficiency; and 3) build systems able to substitute the manual work leading to an improved standardization which would limit the risk of human errors. In this view, automation in the ART laboratory involves multiple issues. It is possible to automate procedures that are usually performed manually by the embryologists. In addition to this, automation involves the introduction of decision support systems, that can help embryologists in making choices. Dealing with embryo culture, thanks to microfluidic technologies, a variety of systems have been developed with the aim of providing culture media changeover, with no need of removing the embryos from their incubators, therefore preventing them from being exposed to environmental conditions. Some of these systems even integrate oocyte insemination and embryo culture so that the whole culture is performed under controlled conditions. Other systems for embryo culture have been built to with technologies able to expose the embryos to microvibrations or gravity that would mimic the mechanical stimuli to which they are exposed in the uterine environment. On the other hand, systems were developed for helping the embryologists in selecting the right embryo for transfer or cryopreservation. In the last decade, time-lapse incubators providing videos of the developing embryos have become more and more popular in the ART laboratories. These systems have been used not only for culturing embryos without displacing them from their environment during the morphological evaluations. Additionally, they have been used as research tools: by observing and annotating morphological features and morphokinetics timings, otherwise impossible to observe in standard incubators, it is possible to point out parameters positively associated to clinical outcomes. According to these parameters, algorithms can be developed with the aim of ranking the embryos within a cohort and predicting their potential for implantation, euploidy or resulting in a live birth. Future improvements can be achieved by image and video analyses via artificial intelligence, combining morphology and morphokinetics to patient clinical features. Machine learning techniques have the potential di uncover new markers for predicting, and therefore improving, the outcome of ART treatments. Other systems capable of supporting the embryologists in embryo selection include culturing platform for the analysis of the spent culture media at a molecular level, to gain important information on embryo metabolism. Many improvements have been recently achieved although extensive research on this field is still needed before the embryo secretome analysis can be efficiently used for clinical applications. Possible future effects of automation could be to lower the costs of ART treatments thanks to a reduced need of space and human resources, equipment, disposables and volumes of culture media, while the parallelization of treatments would increase throughput. Finally, controlled data from standardized treatments would open new research applications and areas that, as a result, will bring to further developments in the field.

WILL BODY-IDENTICAL MHT BECOME THE FIRST CHOICE FOR MENOPAUSAL HORMONE THERAPY?

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Contrary to men, who need to deal only with one lifephase of hormonal turbulence – puberty – women experience a second such turbulent phase of life: perimenopause, which may begin up to 10 years prior to the cessation of menses. During early perimenopause - at the beginning of the menopausal transition – changes in cycle length (> 7 days compared with previous years) start. Late perimenopause is characterized by „skipped“ periods, resulting in cycle lengths of 60 days and more. Early perimenopausal women may complain of intermittent breast tenderness, often followed by prolonged and heavy menstrual bleeding, both due to higher endogenous estrogen production than in premenopausal years. Later, epithelial dryness and atrophy become a problem, exposing eyes, mouth, vagina and also urethra and bladder to increased risk of recurrent infections. To counteract the increased endogenous estrogen of early perimenopause, progesterone would be ideal, due to it's antiestrogenic effect at the pituitary. However, since ovulation rates decline from 60% to 5% in the last seven years before the cessation of menses, progesterone is lacking. Application of progesterone may therefore alleviate several of the perimenopausal complaints, even without estrogen treatment. When low estradiol-production supervenes or if hot flushes and sweating are not sufficiently controlled with progesterone alone, estradiol treatment also becomes increasingly important.

TRANSLATIONAL MEDICINE IN REPRODUCTIVE AGING

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Translational medicine is a rapidly growing discipline in biomedical research and aims to expedite the discovery of new diagnostic tools and treatments by using a multi-disciplinary, highly collaborative, "bench-to-bedside" approach and may apply well to the process of reproductive aging. Reproductive longevity is critical for fertility and impacts healthy ageing in women, yet insights into the underlying biological mechanisms and treatments to preserve it are limited. The human female reproductive lifespan is regulated by the dynamics of ovarian function, which in turn is influenced by several factors: from the basic molecular biological mechanisms governing folliculogenesis, to environmental and lifestyle factors affecting the ovarian reserve between conception and menopause. Anti-Müllerian hormone (AMH), a peptide growth factor of the transforming growth factor-β family, is a reliable marker of ovarian reserve. Serum AMH levels can be affected by environmental and genetic factors. The mechanisms underlying the decline in women's fecundity from the mid-thirties remain to be fully elucidated. The DNA methylation (DNAm) age of most healthy tissues changes predictably with and follows chronological age, but DNAm age in some reproductive tissues has been shown to depart from chronological age. We have successfully developed a granulosa cell clock able to predict the age of both mural granulosa cells and leucocytes. From a broader point of view, global and regional demographic trends play an additional important role in shaping the female reproductive lifespan, and finally, influences on an evolutionary scale have led to the reproductive senescence that precedes somatic senescence in humans. There is now compelling evidence that the inheritance of such genetic information is accompanied by additional epigenetic marks, or stable heritable information that is not accounted for by variations in DNA sequence. The reversible nature of epigenetic marks coupled with multiple rounds of epigenetic reprogramming have made the investigation of this phenomenon challenging.

THE ENDOMETRIOMA AND THE OVARIAN RESERVE: THE CHALLENGE OF THE SURGEON ART BEFORE OPERATION

Edgardo Somigliana, *Italy*

Two decades have passed since the observation that laparoscopic ovarian stripping, the gold standard technique for the removal of endometriomas, can be detrimental to ovarian reserve. In this period, several groups have proposed alternative surgical modalities, with the aim of limiting, if not preventing, this damage. Interesting options have been proposed and are gaining consensus but, to date, these proposals lack robust evidence from large RCTs, and laparoscopic ovarian stripping remains the most employed approach worldwide. Of relevance here is that the scientific community has started to investigate new surgical approaches in the absence of a definitive demonstration of the pathogenetic mechanisms of damage. This is obviously unfair because the knowledge of the modality of damage is an essential prerequisite to plan techniques that can overcome it. In the debate regarding surgery for endometriomas, a new important awareness has grown in recent years. Much attention should indeed be given to the recent definitive demonstration that ovarian reserve is not relevant for natural conception, provided that it is sufficient to ensure regular menstrual cycles. Ovarian reserve is important to ovarian response to hyperstimulation (and therefore for IVF success) but is unremarkable for natural pregnancy seeking. As a matter of fact, if surgery for endometriomas could markedly enhance natural conception (if not restore normal fecundity), the detrimental impact to the ovarian reserve would be of scant relevance. The woman would conceive by herself without the need for IVF. However, is this the case? RCTS are lacking but it is generally believed that the chances of natural pregnancy following surgery for endometriomas in infertile women is below 50%, presumably only 20-30%. Does this justify the possible damage, the longer time to pregnancy and the possible impairment of the chances of success of subsequent IVF? Robust studies investigating the most effective surgical technique for endometriomas are pressingly needed. In the meantime, physicians have to handle information in the wisest manner and tailor therapeutic choices through a process of shared decision-making. The notion that ovarian reserve is unremarkable to natural conception may justify a different vision, i.e. favouring surgery in case of low ovarian reserve and IVF in case of intact ovarian reserve. A variant of this vision could be to start with IVF in all cases to maximally exploit the remnant ovarian reserve, and then shift to surgery in case of failure.

DOES COCHRANE REVIEWS SHOW ANY ROLE FOR METFORMIN IN THE MANAGEMENT OF PCOS?

Thomas Tang, *UK*

Background: Polycystic ovary syndrome (PCOS) is characterised by menstrual disturbance, hyperandrogenism and hyperinsulinaemia. Hyperinsulinaemia occurs secondary to insulin resistance and is associated with increased risk of cardiovascular disease and diabetes mellitus. Insulin-sensitising agents such as metformin may be effective in treating PCOS-related anovulation. ***Objectives:*** To evaluate the effectiveness and safety of metformin in combination with or in comparison to clomiphene citrate (CC) in improving reproductive outcomes. ***Search methods:*** We searched the following databases from inception to Dec 19: Cochrane Gynaecology and Fertility Group Specialised Register, CENTRAL, MEDLINE, Embase, PsycINFO and CINAHL. We searched registers of ongoing trials and reference lists from relevant studies. ***Selection criteria:*** We included randomised controlled trials of metformin compared with placebo, no treatment, or an ovulation-induction agent for ***and analysis:*** Two review authors independently assessed studies for eligibility and bias. Primary outcomes were live birth rate and gastrointestinal adverse effects. Secondary outcomes included other pregnancy outcomes, menstrual frequency and metabolic effects. We combined data to calculate pooled odds ratios (ORs) and 95% confidence intervals (CIs). We assessed statistical heterogeneity using the I^2 statistic and reported quality of the evidence for primary outcomes using GRADE methodology. ***Main results:*** We assessed the interventions metformin, clomiphene citrate, metformin plus clomiphene citrate. We compared these with each other, placebo or no treatment. In total, 45 studies (4552 women) were included in the analysis. ***Metformin versus placebo or no treatment:*** Metformin versus placebo or no treatment The evidence suggests that metformin may improve live birth rates compared with placebo (OR 1.59, 95% CI 1.00 to 2.51; I^2 = 0%; 4 studies, 435 women; low-quality evidence). The metformin group probably experiences more gastrointestinal side effects (OR 4.00, 95% CI 2.63 to 6.09; I^2 = 39%; 7 studies, 713 women; moderate-quality evidence). There are probably higher rates of clinical pregnancy (OR 1.98, 95% CI 1.47 to 2.65; I^2 = 30%; 11 studies, 1213 women; moderate-quality evidence). There may be higher rates of ovulation with metformin (OR 2.64, 95% CI 1.85 to 3.75; I^2 = 61%; 13 studies, 684 women; low-quality evidence). We are uncertain about the effect on miscarriage rates (OR 1.08, 95% CI 0.50 to 2.35; I 2 = 0%; 4 studies, 748 women; low-quality evidence). ***Metformin plus clomiphene citrate versus clomiphene citrate alone:*** We are uncertain if metformin plus CC improves live birth rates compared to CC alone (OR 1.27, 95% CI 0.98 to 1.65; I^2 = 28%; 10 studies, 1219 women; low-quality evidence), but gastrointestinal side effects are probably more common with combined therapy (OR 4.26, 95% CI 2.83 to 6.40; I^2 = 8%; 6 studies, 852 women; moderate quality evidence). The combined therapy group probably has higher rates of clinical pregnancy (OR 1.62, 95% CI 1.32 to 1.99; I^2 = 31%; 19 studies, 1790 women; moderate-quality evidence). The combined group may have higher rates of ovulation (OR 1.65, 95% CI 1.35 to 2.03; I^2 = 63%; 21 studies, 1568 women; low-quality evidence). There was no clear evidence of an effect on miscarriage (OR 1.35, 95% CI 0.91 to 2.00; I 2 = 0%; 10 studies, 1206 women; low-quality evidence). ***Metformin versus clomiphene citrate:*** When all studies were combined, findings for live birth were inconclusive and inconsistent (OR 0.71, 95% CI 0.49 to 1.01; I 2 = 86%; 5 studies, 741 women; very low-quality evidence). In subgroup analysis by obesity status, obese women had a lower birth rate in the metformin group (OR 0.30, 95% CI 0.17 to 0.52; 2 studies, 500 women), while the non-obese group showed a possible benefit from metformin, with high heterogeneity (OR 1.71, 95% CI 1.00 to 2.94; I^2 = 78%, 3 studies, 241 women; very low-quality evidence). However, due to the very low quality of the evidence we cannot draw any conclusions. Among obese women taking metformin there may be lower rates of clinical pregnancy (OR 0.34, 95% CI 0.21 to 0.55; I^2 = 0%; 2 studies, 500 women; low-quality evidence) and ovulation (OR 0.29, 95% CI 0.20 to 0.43; I^2 = 0%; 2 studies, 500 women; low-quality evidence) while among non-obese women, the metformin group may have more pregnancies (OR 1.56, 95% CI 1.06 to 2.29; I^2 = 26%; 6 studies, 530 women; low-quality evidence) and no clear difference in ovulation rates (OR 0.80, 95% CI 0.52 to 1.25; I^2 = 0%; 5 studies, 352 women; low-quality evidence). We are uncertain whether there is a difference in miscarriage rates between the groups (overall: OR 0.92, 95% CI 0.51 to 1.66; I^2 = 36%; 6 studies, 781 women; low-quality evidence) and no studies reported gastrointestinal side effects. ***Conclusions:*** Our updated review suggests that metformin may be beneficial over placebo for live birth however, more women probably experience gastrointestinal side effects. We are uncertain if metformin plus CC improves live birth

effects are probably increased with combined therapy. When metformin was compared with CC, data for live birth were inconclusive, and the findings were limited by lack of evidence. Results differed by body mass index (BMI), emphasising the importance of stratifying results by BMI. Due to the low quality of the evidence, we are uncertain of the effect of metformin on miscarriage in all three comparisons. An improved clinical pregnancy and ovulation rate with metformin and clomiphene citrate versus clomiphene citrate alone suggests that combined therapy may be useful although we do not know whether this translates into increased live births.

DUO-STIM ADVANTAGES AND DISADVANTAGES: PRO

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The personalization of IVF treatment is key in a modern clinic to maximize both efficacy and efficiency. In this context, we should move from evaluating each cycle per se to a more comprehensive vision of the whole treatment. From this perspective, efficiency involves even reducing the burden represented by complications, such as absence of transferable embryos, implantation failure, miscarriage and increasing time loss. In fact, all these factors might in turn increase patient drop-out. The technical improvements in IVF (e.g. blastocyst culture, single embryo transfer (SET), cryopreservation of oocytes/embryos, preimplantation genetic testing for aneuploidies (PGT-A), freeze-all) allowed the implementation of non-conventional controlled ovarian stimulation (COS) protocols for oncologic and poor prognosis patients in IVF. However, the current theory states that several waves of follicular recruitment might arise throughout the ovarian cycle this opened the possibility of non-conventional COS protocols outside the fertility preservation context. Beyond the random start approach, at least three more non-conventional COS protocols involve a stimulation starting in the luteal phase of the ovarian cycle: late follicular phase stimulation (late-FPS), luteal phase stimulation only (LPS-only) and double stimulation in the same ovarian cycle (FPS plus LPS, or DuoStim). These non-conventional COS protocols have been adopted across the last decade to treat poor prognosis women and/or patients of whom time to oocyte retrieval is critical. Using LPS in the same ovarian cycle 5 days after ending FPS (i.e. DuoStim), represents the most promising non-conventional protocol to treat poor prognosis women, as consistently reported from several groups worldwide. Moreover this protocol has been successfully adopted also for fertility preservation where the time is crucial. The rational of DuoSTim approach is to increase the number of oocytes and embryos available per menstrual cycle in all patients where obtaining competent oocytes is a urgent task for malignant diseases or other medical indications and in patients with advanted maternal age and/or reduced ovarian reserve such as patients fulfilling Bologna Criteria. The number of oocytes retrieved, in fact, together with the age of the patient is one of the most important factor to predict the live birth of an healthy baby. Based on the studies already published, DuosTim protocol is an alternative option for increasing number of MII oocytes retrieved and of the blastocysts obtained in short time frame increasing the efficacy of an IVF procedure without compromise the oocytes competence coming from anovulatory waves. Indeed, exogenous gonadotropins started in follicular or in luteal phase, seems not significantly modify the fertilitation and blastulation rate as well as the likelihood of aneuploidy embryos in patients undergoing COS. Observation studies showed that DuoStim is not superior to two conventional COS protocols in terms of CLBR per ITT. However, DuoStim strategy lessens the patient drop-out rate, which is highly likely after a failed attempt with conventional COS in specific patients population. Indeed, treatment drop-out, especially in poor prognosis patients (AMA and POR), is very high and the reason is not just their prognosis, but includes also financial, psychological and logistic aspects. On the other hand, LPS provides these patients with a higher chance to obtain and transfer an euploid blastocyst in the same ovarian cycle. For this reasons, in freeze-all cycles, DuoStim represents a reasonable alternative to oocyte accumulation, which can be even proposed also underway. Of note, the choice to start immediately a second stimulation shall follow a careful counseling focused on patients' chance to find at least one euploid embryo on account of their age and of the number of blastocysts obtained after conventional stimulation. Cost-benefit analyses are required from future trials. However, until such evidences can be produced, the autonomous informed choice of the patients to undergo a DuoStim protocol should not be questioned, especially after a thorough and careful counseling of its pros, cons, and putative alternatives. Finaly, DuoStim protocol is confirmed a feasible and efficient approach also from clinical, obstetric and perinatal perspectives, targeted at patients who need to reach the transfer of an euploid blastocyst in the shortest timeframe. Moreover, all results coming from DuoStim protocol encourage additional clinical studies and research to further personalize COS in specific populations of patients such as poor prognosis patients, many of whom may benefit from non-conventional protocols. This evidence should be confirmed in future RCT , long-term follow-up of the babies born after LPS are advisable.

SHOULD WE BE USING EXPANDED GENETIC SCREENING IN ALL PATIENTS? YES

Rita Vassena, *Spain*

In this interesting and timely debate I will defend the position that expanded carrier screening (ECS) should be used in all IVF patients. ECS is defined as the screening for several mutations on dozens of genes, which are causative of monogenic disease of recessive and X-linked inheritance pattern. While carrier screening in an old concept and has been widely accepted for some disease present with high frequency in certain populations (for instance cystic fibrosis or thalassemia), it has historically been proposed to a limited number of at-risk individual. My argument for the necessity of offering ECS to all couples is based on several lines of reasoning: i) the observation that most children affected by recessive genetic diseases are born to families without a history of disease ii) that most genetic diseases detectable at birth are preventable through ART means iii) that the growing tendency to populations to mix will eventually make ethnicity based recommendations less useful, and that iv) the cost of screening for several diseases is now comparable or even lower than screening for just 1 or 2, possibly making these test cost-effective over targeted screening.

E-POSTER ABSTRACTS

INFERTILITY/ART/IVF

FERTILIZATION FAILURE AND BLASTOCYST FAILURE: IS PIEZOELECTRIC ACTIVATION AN ALTERNATIVE?

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Problem statement: Egg activation triggers stimulation with sperm as a result of fertilization, creating long-termCa+2 fluctuations and activating the release and transport of Ca+2. These Ca+2 fluctuations continue until the pronuclear formation and facilitate early embryo development. Piezoelectric microinjection is a method in which an increase of Ca+2 is performed by delivering a certain level of electric current to the eggs after the operation. During fertilization, when the sperm attaches to the zona pellucida, specific receptors in the acrosome are activated and exocytosis occurs. When sperm penetration occurs, intracellular Ca+2 concentration increases, and Meiosis II is completed. ***Methods***: The sibling group consisting of 31 patients was selected, and all of the patients in the group had an indication of fertilization failure or blastocysts failure in at least 2 previous cycles. Only the ICSI procedure was applied to half of the eggs obtained from the patients. For the second group, electric activation applied 30 minutes after the ICSI process. The eggs are placed in a buffer solution between two electrodes created in a Micro Dish with 0.5 mm intervals, and a certain level of electricity is given to the eggs with the Electro Manipulator. ***Results***: The average age of the patients in our study was 35.29, the average number of IVF cycles without fertilization was 3.8, and the average of cycles without blastocyst was 4.7. According to the results, fertilization rate of 38%, blastocyst rate of 0.09%, and euploid blastocyst rate of 25% were found in the control group without piezo electric activation. In the electrically activated group, 82% fertilization rate, 48% blastocyst rate, and 66% euploid blastocyst rate were obtained. A clinical pregnancy rate of 55% was also determined in the electrically activated group. ***Conclusion***: It was determined that ultra-structural damage was reduced to a very minimum in eggs that underwent the piezoelectric method. Piezo electric method features give valuable results for advanced age patients in the total fertilization failure and blastocyst failure group. It was determined that the method was more effective than other activation methods and we achieved high clinical pregnancy rate.

VITRIFIED DONOR EGG TRANSPORT: NEW CONCEPT OF EGG DONATION AFTER COVID-19 PANDEMIC?

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Problem statement: Interest in frozen donor eggs has increased especially due to the difficulties in the travelling of patients awaiting treatment after the Covid-19 pandemic. The fact that the number of egg donors is insufficient, legal regulations are restricting the use of fresh donor oocytes, and patients cannot find adequate numbers and appropriate donor profiles have made egg-banking more important. ***Methods***: In our study, we conducted a general analysis of survival, cleavage and blastocyst rates of vitrified donor eggs in 40 different clinics. In addition, the number of clinics using vitrified donor eggs after the Covid-19 was compared to the pre-pandemic period. The aim of our study was to show the direct effect of the egg-banks on ART performance in different countries, as well as evaluate possible increase in egg donation cycles after the Covid-19 pandemic. ***Results***: The data obtained through egg-banking initially included 30492 frozen donor eggs. Post-thawing survival rate reached 89.96%; average fertilization rate was determined to be 84.22%; blastocyst utilization on the 5th and 6th days comprised 44,52%. We calculated that frozen donor eggs were sent 171 times to 64 clinics from 27 countries in the part of 2020 until the pandemic period and all these shipments were successfully completed. During the Covid-19 pandemic in the last 3 months of 2020 and the first month of 2021, frozen donor eggs were successfully sent 96 times to 40 clinics from 21 countries. Frozen donor egg circulation during Covid-19 period was compared to circulation in the same period of 2019. In the last 3 months of 2019 and the first month of 2020, 5219 frozen donor eggs were sent to 31 clinics in 18 countries; and based on the last 3 months of 2020 and the first month of 2021 (Covid-19 pandemic period), 6874 frozen donor eggs were sent to 40 clinics from 27 countries. ***Conclusions***: Frozen donor oocyte usage became more effective during Covid 19 pandemic. Egg Banking can supply more alternative for donor profiles, high quality morphological donor egg and better outcomes for egg donation cycles. There is no risk or potential damage to frozen donor eggs during transportation.

CASUAL DIAGNOSIS OF QUIMERA IN A MAN WITH FERTILITY PROBLEMS

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Introduction: By definition, a chimera is produced by the fusion of two different zygotes in a single embryo. It is a rare chromosomal disorder in humans. Sex-chromosome discordant chimerism in humans (XX/XY chimerism) is a rare chromosomal abnormality. Its incidence is still unknown. The XX/XY chimera manifests variable genital phenotypes, ranging from normal male or female genitalia to different degrees of ambiguous genitalia. Therefore, genotyping of XX/XY chimeras is important not only to clarify its developmental mechanism but also for diagnosis and treatment, as such patients occasionally present with fertility problem. ***Methods:*** We report a 34- years old male with no medical or surgical history. Man fenotype, normal physical exploration. He and her partner were being studied in Human Reproduction Unit because of primary sterility. He has normal analysis. Seminogram showed criptozoospermia, second seminogram showed isolated sperm. A kariotype was requested which result was: 46XX, inv(9)(p11q13)[42]/46XY[7] The metaphases analyzed with a resolution of 400 bands show two cell lines, both normal but with different sex chromosome composition, a minority (15%) with male sex chromosomes (XY), and another with female sex chromosomes (XX) (85 %) that also presents an inversion of the heterochromatic block of one of the chromosomes of pair 9, it is considered an extreme of the normal variability of the karyotype, a polymorphism compatible with normality.It is concluded that it is a chimerism caused by the fusion of two different zygotes. ***Conclusion:*** It was a casual diagnosis of chimera because of de sterility and a pathological seminogram. It is interesting because it is an really uncommon chromosomal abnormality. In order to have more information about the quimera we would like to take some buccal tissue, nails tissue and blood sample in order clear and study deeply the XX/XY ratio in the different tissues of the body. We will also make an abdominal ultrasound in order to clarify the

presence or absence of ovaries or ovarian tissue.

LOW SERUM PROGESTERONE LEVELS THE DAY PRIOR TO THE TRANSFER OF FROZEN EMBRYOS AND THE PREGNANCY RATE

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Objective: To determine the association between serum progesterone levels the day before frozen embryo transfer (FET), and the rate of pregnancy and spontaneous abortion in artificial cycles. ***Material and methods:*** This was a prospective cohort study which included 156 artificial cycles performed at the Reproduction Unit of a tertiary hospital between January and October 2020. Endometrial preparation was performed by administrating oral or transdermal estrogens from the first day of the menstrual cycle. Serial ultrasound scans on follow up were carried out and,when a three-layered pattern endometrium with a thickness of 7 mm or more was achieved,vaginal progesterone (200 mg / 8 h) was started for either 5 or 3 days if blastocysts or pre-embryos were to be transferred, respectively. The morning before the FET day serum progesterone levels were determined and 14 days later, bHCG levels were tested. ***Results:*** The pregnancy rate in artificial cycles was 39.7% and the spontaneous abortion rate was 14.1%. There were no significant differences in progesterone levels between patients who achieved pregnancy (10ng / ml) from those that did not (10, 5ng / ml), (p = 0.262). In order to eliminate the possible confounding factor of poor quality embryo on the pregnancy rate, analysis was stratified by embryo quality following the ASEBIR classification, however, no significant differences were found. The cut-off point for progesterone levels in our population, for a sensitivity of 80%, was 8.5ng / ml, with no significant differences in pregnancy rates. However, those who had a miscarriage had lower progesterone levels (10.8ng / ml) compared to those with an on-going pregnancy (11.6ng / ml) (p = 0.187). The spontaneous abortion rate was lower with progesterone levels 8.5ng / ml (p = 0.157). These differences were not significant, most likely due to the small sample size. ***Conclusions:*** Serum progesterone levels are not a good predictor of pregnancy rate. We did not find better pregnancy rates in women with higher serum levels of progesterone however we did find a higher abortion rate in women with progesterone levels ≤ 8.5 ng / ml.

ADENOMYOSIS AND IN VITRO FERTILIZATION. SYSTEMATIC REVIEW AND META-ANALYSIS OF THE EFFECTS OF ULTRALONG OR MODIFIED ULTRALONG AGONIST PROTOCOL ON REPRODUCTIVE OUTCOMES

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Problem statement: Adenomyosis is a benign uterine disorder in which endometrial glands and stroma are located within the myometrium causing uterine bleeding, pain and infertility. Previous meta-analyses have addressed a deleterious effect of adenomyosis over In Vitro Fertilization (IVF) results. ***Methods***: Systematic review with meta-analysis of studies conducted following PRISMA guidelines assessing the IVF results in patients with adenomyosis compared to controls and studies comparing the effects of ultralong or modified ultralong protocol with standard agonist protocol for ovarian stimulation prior to IVF inpatients with adenomyosis. ***Results*****:** After a systematic search using MEDLINE, PubMed, EMBASE, Web of Science, Cochrane and main international Trial Registries, 668 studies were retrieved of which 60 were assessed for eligibility. Twenty-one observational studies were included in the qualitative review and nineteen in the meta-analysis, involving reproductive outcomes from 8660 patients. Sixteen studies assessed the effect of adenomyosis on IVF results. Live birth rate after IVF was significantly reduced in patients with adenomyosis (OR=0.62; 95% CI, 0.43-0.90; 9 studies, 5207 patients). Clinical pregnancy rate was also significantly reduced (OR=0.65; 95% CI, 0.51- 0.82) and miscarriage risk was significantly increased (OR=1.74; 95% CI, 1.10-2.75). When results were adjusted by age, live birth rate remained significantly reduced (OR=0.77; 95% CI, 0.64-0.92; 7 studies), clinical pregnancy was also significantly lower (OR=0.73; 95% CI, 0.57-0.93; 11 studies) and the miscarriage rate was significantly increased (OR=1.99; 95% CI, 1.07-3.68; 11 studies). Four studies assessed the potential effect of long term down regulation with GnRH before IVF treatment. Live birth, clinical pregnancy and miscarriage rates after ultralong or modified ultralong agonist protocol for downregulation were not significantly different compared to the long agonist protocol***. Conclusion:*** Adenomyosis is significantly associated with a lower chance of live birth and clinical pregnancy and a higher risk of miscarriage after IVF even after adjusting for confounding factors as age. Live birth and clinical pregnancy rate were not significantly different after ultralong or modified ultralong agonist downregulation protocol. The potential beneficial role of this therapy needs to be properly assessed in randomized controlled studies.

DOES INDIVIDUALISED AMH AND BMI ADJUSTED DOSE OF FOLLITROPIN DELTA FOR OVARIAN STIMULATION MINIMISE OVARIAN HYPERSTIMULATION SYNDROME RISK IN HYPER-RESPONDERS?

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Ovarian hyperstimulation syndrome (OHSS) is a significant adverse event of assisted reproductive technology (ART) cycles resulting in maternal morbidity. In the UK, it is a mandatory requirement to report severe/critical OHSS incidents to the national regulatory body. Follitropin-delta has recently gained momentum for use in controlled ovarian stimulation (COS) during ART cycles as its dose can be individualised for a woman based on her body mass index (BMI) and AMH using an algorithm. In hyper-responders at higher risk of developing OHSS, there is lack of evidence regarding ability of individualised dosing with follitropin-delta in minimising OHSS. ***Aims:*** Does BMI and AMH adjusted individualised dosing of follitropin delta minimise risk of OHSS in hyper-responders during ART cycles? ***Methods****:* A service improvement retrospective review was performed on data spanning July 2020 to August 2021. Women undergoing ART cycles with BMI ≤30, AMH ≥30 pmol/l and/or antral follicle count of 30 (referred to as hyper-responder group) met the eligibility criteria. Data from women on individualised dose of follitropin-delta (RekovelleTM) for COS were compared with women, who were on highly purified human menopausal gonadotrophins, hMG (MenopurTM). Primary outcomes were number of oocytes retrieved and OHSS rates. Secondary outcomes were number of follicles aspirated, oocyte recovery rate, oocyte maturation rate (Metaphase II oocytes), fertilization rate and. 'Freeze-all' rates to mitigate OHSS risk. ***Results:*** Of 119 participants, 57 had follitropin-delta whilst 62 had hMG with median age ± Standard deviation (SD) of 32 (±3.8) and 33.5 years (±4.5)

respectively. Mean number of follicles ±SD in follitropin-delta group was 19.2 ± 8.4 (95% CI 17.1-21.4) vs 18.4 ± 7.9 (95% CI 16.4-20.4); p=0.29. Mean number of oocytes retrieved in follitropin-delta group was 14.2 ± 9 (95% CI 11.8-16.5) vs 11.6 ±6 in hMG group (95%CI 10.0-13.2). OHSS rate was not statistically significant between the two groups.

Outcome	Follitropin delta (Rekovelle) Mean % (± SD)	hMG (Menopur) Mean ± SD	Odds Ratio (OR)	95% Confidence Interval (CI)	p value
Oocyte Recovery Rate	62% (± 24)	64% (± 24)	0.91	0.51-1.63	0.62
Oocyte Maturation Rate	85% (± 15)	84% (± 17)	1.07	0.50-2.32	0.7
Fertilisation Rate	62% (± 25)	56% (±25)	1.28	0.73-2.25	0.38
Failed Fertilisation Rate	3.5%	4.8%	0.71	0.12-4.44	0.7
Freeze All Rate	21%	3%	7.82	1.67-36.71	0.009
Total OHSS rate (outpatient and inpatient)	35%	29%	1.32	0.61-2.86	0.47
OHSS rate in those requiring admission (inpatient)	7%	10%	0.79	0.21-3.02	0.7

Conclusions: Individualised dose of follitropin-delta for COS during ART cycles for hyperresponders has comparable ovarian response to hMG and can be an alternative for risk minimisation strategy for OHSS. However, further research is warranted to assess its clinical & cost effectiveness and safety profile in randomised controlled trials in hyper-responders.

DOI: *Ferring-travel-grant-to-attend-meetings*

IMPACT ON THE REPRODUCTIVE RESULTS OF THE GENOMIC STUDY OF SPERM DNA FRAGMENTATION

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Problem statement: Sperm DNA fragmentation is the frequent common genetic alteration in spermatozoa. It is pathological when the rate exceeds 30%. It is due to the increase in free radicals and oxidative stress, related to age and lifestyle; which cause defects during spermatogenesis. An impact on reproductive outcomes has been described, increasing the rate of miscarriages, and decreasing the success of assisted reproductive techniques (ART). Formerly, treatment was based on sexual abstinence, but it has been shown that a pattern of 2 to 4 ejaculations per day, minimum 14 days, could improve sperm viability by reducing free radicals and fragmentation rate. ***Method:*** The study was conducted at the Hospital Insular Materno-Infantil de Canarias between January 2015 and June 2021. It was hypothesized that the pattern of repeated ejaculations should be maintained for at least 2 months, since this is the period occupied by spermatogenesis. Inclusion criteria were: Couples with fertilization problems, no embryo progression after ART, or after 2 unsuccessful in vitro fertilization cycles and no other justifying cause. Exclusion criteria were: Loss to follow-up or pregnancies achieved with gamete donation. ***Results:*** Thirty-seven men were included, whose mean age was 36.2 years. 13.5% were smokers and 5.4% had chronic arterial hypertension. At least one miscarriage had occurred in 10.8% of the couples. Seminogram alterations were found in 35.13% of men, with 10.8% having oligozoospermia, 8.1% asthenotherozoospermia, 8.1% oligotherotherozoospermia, 5.4% cryptozoospermia, 2.7% asthenozoospermia and 2.7% hypospermia. The mean fragmentation rate before treatment was 87.4%, and after treatment, it decreased to 24.6%. The mean reduction was 62.8%. Of the couples, 48.6% achieved gestation, of which 13.5% were spontaneous and 16.2% after assisted reproduction technique. The rest were achieved in a private center or after gamete donation. ***Conclusion:*** After at least 2 months of frequent ejaculations, a reduction in the sperm DNA fragmentation rate of more than 60% was observed. In one third of the couples who complied with the therapeutic plan, gestation was achieved spontaneously or after assisted reproduction technique.

DELAYED DECISION-MAKING TO TAKE IVF PROGRAM AMONG INFERTILITY COUPLES IN DEVELOPING COUNTRIES: A SCOPING REVIEW

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Problem statement: Almost 180 million people around the world experience infertility, and most of those people live in developing countries. Nowadays, IVF services has become available in developing countries, but the proportion of couples seeking medical care was still lower compared with developed countries and the proportion of people actually receiving care was substantially less. This study aims to determine the barriers that cause delaying to take IVF program among infertility couples in developing countries. ***Method:*** A scoping review was conducted using the Population-Concept-Context (PCC) framework by the Joanna Briggs Institute. We searched five electronic databases for published articles and additional search strategies (snowballing literature search and citation tracking). Comprehensive literature searches and study selection were conducted by two authors, data extraction were finalized by discussion with other authors. ***Result:*** There were eleven included articles in our scoping review, and the country origin represents the developing countries from throughout the world. The qualitative study was the most widely used study design in these sources of evidence. The cost of the IVF program was the most mentioned from included studies in our scoping review to be the greatest barrier. Limited access and less of ARTs center, lack of qualified infertility trained staff, no government subsidy or support, the government policy and priority, sociocultural, religion and myths were also being majority obstacles among infertility couples in low-income countries. ***Conclusion:*** The high cost of IVF services is the main barrier on infertility treatment that cause delays in IVF programs in developing countries. Thus, the affordable, acceptable and effective IVF program is needed for infertility treatment.

Keywords: *in vitro fertilization, assisted reproductive techniques, assisted reproductive technologies, barriers, developing countries, low-income countries.*

DEVELOPMENT OF A NEW DEVICE FOR AUTOMATIC VITRIFICATION OF OOCYTES

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Problem statement: Vitrification is a technique used daily in assisted reproduction clinics for the cryopreservation of oocytes and blastocysts which provides good results. The most used methodology worldwide is the Kitazato protocol, which has reported the best survival rates. The manual procedure can be variable between clinics and users in the same centre and is not free from human error, which leads to low replicability from one protocol to another. The aim of developing an automated vitrification device using Kitazato vitrification/warming medium is to eliminate possible errors and variability between users and so that, what is vitrified in one centre can be warmed in another and vice versa. This would optimize the protocol, achieving better results and the same survival rates, regardless of the centre where the technique has been performed. ***Methods:*** The automated device and the microfluidic chip were designed by our team.

We used 235 mouse zygotes (to mimic oocyte behaviour because of their greater availability and similar characteristics) divided into 2 groups: A) Automated protocol (n=132); B) manual control group according to Kitazato protocol (n=103). ***Results*:** A chi square test was performed in order to compare survival rates between protocols, that were the following: A: 97.90%; B: 99.00%. No statistical differences were found between groups. ***Conclusions:*** Our device for the automation of oocyte vitrification offers promising results on survival rates and similar to manual protocols routinely used in IVF laboratories. The use of an automated device could lead to homogenization of results across assisted reproduction clinics, thus avoiding human error and variability between centres.

KISSPEPTIN – A POTENTIAL OOCYTE MATURATION TRIGGER FOR IN VITRO FERTILITATION

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Problem statement: Despite the fact that GnRH plays a pivotal role in controlling reproductive functions, kisspeptin has recently emerged as a key regulator of the HPG axis. Peripheral administration of different isoforms of kisspeptins (kisspeptin-10 and 54) has been shown to stimulate GnRH and gonadotropin release and to activate the LH surge required for oocyte maturation and ovulation in animal studies. Since animal and human studies have suggested that the peripheral administration of kisspeptin-10 and 54 is involved in the generation of the LH surge, it was hypothesised that exogenous kisspeptin could be used to trigger oocyte maturation in women with subfertility undergoing IVF treatment. ***Methods:*** This paper presents a review of literature with the current information about kisspeptins as a potential oocyte maturation trigger in IVF procedures. Papers published in the last 10 years (between 2010 and 2020) were included in this review. ***Results:*** Recent studies investigated the potential for kisspeptin as a novel method of triggering oocyte maturation in women undergoing IVF. In a recombinant FSH/GnRH antagonist IVF protocol, a single subcutaneous injection of kisspeptin-54 was used as an oocyte maturation trigger. Fertilisation occurred in 92% of cases, with biochemical and clinical pregnancy rates of 40% and 23%. Kisspeptin-54 may be used efficiently to trigger oocyte maturation in women at high risk of developing OHSS. In a randomised clinical trial of 60 women following a standard recombinant FSH/GnRH antagonist protocol, where a single injection of kisspeptin-54 was used to trigger oocyte maturation, the achieved pregnancy rates compared with currently used pharmacological triggers of oocyte maturation. ***Conclusions:*** Peripheral kisspeptin administration could be used as a promising method of triggering oocyte maturation in women undergoing IVF treatment due to its efficacy estimated through pregnancy rates when compared to pharmacological triggers currently in use. Furthermore, kisspeptin may also be administered effectively and safely to trigger oocyte maturation in patients at high risk of developing OHSS. Further research with larger studies will be required in the future to determine the clinical utility of kisspeptin, establish the optimal trigger of oocyte maturation, and to improve the reproductive outcome for women undergoing IVF treatment.

SUBTLE CHANGES IN PERIVASCULAR STROMAL STEM CELLS AFTER LOCAL ENDOMETRIAL INJURY

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Problem statement: One often used adjunct therapy for recurrent implantation failure (RIF) is to generate a local endometrial injury (LEI) also known as endometrial scratching. We wondered about the role of perivascular stromal stem cells (pSSC) which mediate cyclic regeneration of the endometrium, allowing it to adapt to local injury by enhancing their stem cell role in stromal vascular tissue regeneration. Accordingly, we aimed to investigate the impact of LEI on pSSC and determine if LEI alters their proportion and/or affected their decidualization. ***Methods:*** Consecutive paired mid-luteal phase endometrial biopsies were obtained from patients with RIF. The biopsies were digested into single cells with the proportion of SUSD2-expressing cells, compared and sorted out using magnetic beads. Under hypoxic condition of 5% oxygen, we compared the CFU-assays and cell expansion of the SUSD2+ve fraction between the 2 samples. Decidualization was also carried out, with produced prolactin and IGFBP-1 levels compared. ***Results:*** Thirty-two participants were recruited with 26 successfully paired samples. The mean age of the participants are 35.3±3.2yrs old. There is no significant change in the proportion of SUSD2+ cells at the first pipelle biopsy (before LEI, 8.69±9.8%) compared to the second (8.64±8.0%) ($p = 0.78$). Cloning efficiencies were 14.7±12.4% and 19.4±17.8%, respectively for SUSD2+ cells obtained from 1st and 2nd LEI, with a non-significant p-value of 0.37, indicating similarity between consecutive biopsies. Using ELISA, prolactin secretion from SUSD2+ cells from the first LEI was 4.19±1.5 times higher than that from the second LEI culture supernatants (p-value:0.008). The same decrease was also observed in expression of IGFBP-1, where there is a 11.5±7.9 fold decrease (p-value:0.04). This difference is corroborated with qPCR where a marked decrease in mRNA expression of prolactin and IGFBP-1 was determined (Paired t-test: p0.001 and p=0.009 respectively). ***Conclusion:*** In this study, we show that a mid-luteal LEI altered the decidualization capacity of pSSC in women with RIF, although it did not alter the proportion or clonogenicity of pSSC. In view of the potential of LEI to improve IVF outcomes in women with RIF, additional investigation is needed to understand the impact of this alternation in decidualization response.

TWIN ECTOPIC GESTATION

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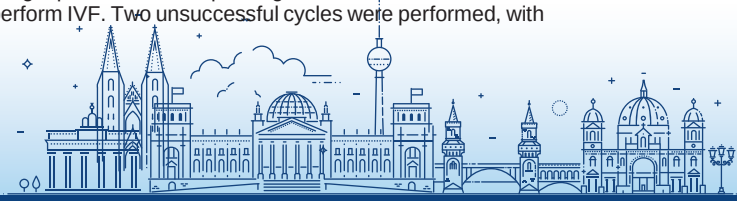
Introduction: Unilateral twin ectopic gestation is an extremely rare entity. ***Problem statement:*** incidence of 1/20,000-250,000 pregnancies ***Case Report:*** We presented a 33-year-old woman with no personal or family history who came to the first visit for primary infertility of 2 years of evolution. Physical examination was normal with both ovaries with 5 antral follicles. Male, 42 years old, with hypertension under treatment. Complementary tests were carried out on both ovaries, showing pathological EMR and oligospermia in the spermogram, so it was decided to perform IVF. Two unsuccessful cycles were performed, with



the transfer of one blastocyst and two pre-embryos. Finally, a new attempt was made with a natural cycle with the transfer of two pre-embryos. At 20 days, 6 weeks after the date of the last corrected period, she went to the emergency department for abdominal pain. On examination, a painful abdomen was observed with no signs of peritoneal irritation, normal gynaecological examination and on transvaginal ultrasound adjacent to the right ovary two anechoic formations of 12x13 mm and 15x17mm, one of them with a vitelline vesicle inside, free perianexial liquid and heterogeneous material suggestive of organised clots. BHGC 11501 mUI/ml was performed. Urgent laparoscopy was indicated and a right salpinguectomy was performed. ***Discussion:*** Ectopic pregnancy is the main cause of maternal morbidity and mortality in the first trimester and its incidence increases with ART The most common type of twin ectopic pregnancy is heterotopic (1/7000 pregnancies. Unilateral twin ectopic gestation is an even rarer entity with few cases reported in the literature. There are clear guidelines on the management of singleton ectopic pregnancies, no such recommendations exist for multigestational ectopic pregnancies. The risk of rupture is higher in this type of gestation, estimated at 30-50%. Surgical intervention remains the mainstay of treatment (3). ***Conclusion:*** Ectopic gestation is a rare but increasing entity due to the increased use of ART. Its management remains a challenge for practitioners.

IMPORTANCE OF ENDOCRINOLOGICAL EXAMINATION IN SUCCESSFULNESS OF IVF TREATMENT

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Problem statement: More than 40 years ago IVF treatment has been introduced for tubal infertility. Last decades, indication of IVF has been extended to more disorders, endocrinological disorders included. Ovulatory dysfunction associated with endocrine diseases is a common leading or associated cause of female infertility, but at optimal reproductive age causal or ovulation induction treatment can usually settle fertility. The leading indications for IVF treatments are currently andrological and originated from age-related ovarian infertility, but other accompanying endocrine dysfunctions affect treatment outcomes. Detailed endocrinological assessment has crucial role in successful infertility treatment. ***Methods:*** During aptitude tests prior to the IVF program, from the leading indication independently, a detailed endocrinological examination was performed in 231 women (mean age 34 years). The studies of hypothalamic and ovarian function, thyroid function and thyroid autoimmunity, adrenal function, carbohydrate metabolism and insulin resistance were covered. In addition to the incidence of each endocrine disease, the frequency of their association was analyzed. ***Results:*** Endocrinological parameters and data was analyzed in 231 cases. The distribution of IVF lead indications was in line with the international trends, was endocrine nature in 87 cases (37.6%, decreased ovarian reserve in 55 cases and chronic anovulation in 32 cases). Associated endocrine abnormalities were found in 141 cases, for a total of 161 women was affected by endocrine dysfunction (69.7%, mean age 35 years). Endocrine dysfunctions incidence in order of frequency: thyroid dysfunction (32.5%), diminished ovarian reserve (23.8%), thyroid autoimmunity (22.5%), polycystic ovarian syndrome (15.6%), insulin resistance (22.5%), obesity (23.8%), hyperprolactinemia (13.4%). The endocrine disease associations were found in all of the cases above. Hypogonadotropic hypogonadism occurred in two cases; congenital adrenal hyperplasia occurred in one case. No endocrine abnormalities were found in 70 cases (30.3%). ***Conclusion:*** Our study confirms the cumulative appearance of endocrine dysfunctions and frequent association in IFV participants with any lead indication. The detailed endocrine examination and proficiency/skill in reproductive endocrinology of IVF practitioners may contribute to IVF treatment success.

CRISPR-CAS9 AND IVF: REVISITING HE JIANKUI`S EXPERIMENT

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***Problem statement*:** The world`s first experiment that brought IVF and CRISPR gene editing technologies together resulted in the jailing of He Jiankui and his core scientific team. Amidst the controversy the clinical data about the two twins at the centre of the experiment, Lulu and Nana, were never published. ***Methods*:** Ethnographic and archival. As a cultural anthropologist I interviewed key people involved in Dr. He Jiankuai`s experiment. Laboratory personnel allowed me to review original clinical data from the birth of Lulu and Nana, as well as their genome sequences. ***Results*:** Lulu and Nana were born by emergency cesarean section at thirty-one weeks of age. Both had Apgar scores of 8. These results were first published in October 2020 in my book, The Mutant Project: Inside the Global Race to Genetically Modify Humans (St. Martin`s Press). I am keen to discuss these findings with the COGI community. ***Conclusion*:** He Jiankui misled the scientific community when he claimed these twins "came crying into the world as healthy as any other babies," with his unconventional announcement on YouTube. When this video was recorded, both babies were actually in a neonatal intensive care unit. At this point it is unknown if the premature birth was the result of known risks of an IVF pregnancy with twins, or an unknown risk of genome editing with CRISPR-Cas9. The blood cells of the twins were also not tested by the He Laboratory to see if they were resistant to the HIV virus. As a social scientist I also studied the values that shaped this experiment. In contrast to much of the public reporting, I found that a vast network of international scientists, investors, and Communist Party officials supported the He Laboratory. I found that market values--focused on speed and disruptive innovation--drove the experiment forward. The targeted CCR5 receptor was selected in recognition of how HIV is an ongoing social problem in China--associated with shame and stigma. The laboratory did follow international norms regarding participant consent, even though the significance of the world`s first CRISPR experiment was downplayed to couples who volunteered.

ENDOMETRIAL SCRATCHING WITH ANALYSIS UTERINE NATURAL KILLER AND PRP (PLATELET RICH PLASMA) INCREASE EMBRYO IMPLANTATION RATE

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Problem statement: Endometrial scratching is technique proposed to facilitate embryo implantation and increase probability of pregnancy in women undergoing in vitro fertilization (IVF). Endometrial immune reaction that occurs in women during implant window is crucial for implantation. Under physiological conditions, uNK lymphocytes are not spontaneously cytotoxic. However, uNK cells are not the only ones in the endometrium: in a predominantly Th1 environment, dendritic cells and Treg cells can increase the uNK lymphocytes cytotoxicity and in turn they are able to recognize trophoblastic cells as non -self and reject them by inducing a missed implant and repeated abortions. When uNK lymphocytes are elevated, aggressive environment is produced in the endometrium causing implantation failure. An altered immune system can be linked to abortions or repeated failures of embryonic implant so a balanced local immune biological reaction is necessary

to allow the embryo adhesion phase. ***Methods:*** Our study includes 180 patients with IVF failures that underwent an endometrial scratching performed with a Pipelle in pre-ovulatory and secretory phase of menstrual cycle and subsequently immunohistochemical examination for uNK cells. The samples were fixed in formaldehyde and were immunohistochemically stained for CD16 Unk cells, CD56 uNK cells and CD138-positive. Research of uNK lymphocytes was performed by histological examination. Immunohistochemical markers CD16 and CD56 reveal the possible presence of lymphocyte elements in the stroma of the endometrial mucosa. Instead, the morphological and immunohistochemical marker CD138 reveals the possible presence of plasma cells that can be evidence of endometritis. ***Results:*** The cutoff considered was 10 CD cells in proliferative phase and 20 cells in secretive phase. CD16 and CD56 cell abundance in proliferative endometrial tissue of women with reproductive failure has suggested they may play a role in this pathogenesis. Common treatment for women with abnormal endometrial NK cells numbers is use of corticosteroids and in addition we use PRP performed 48 hours before the embryotransfer. Pregnancy rate was significantly higher (43%) in the same group of patients under 40 with several previous IVF failures (20% in control group). ***Conclusion:*** Performing this combined treatment, endometrial scratching and PRP, in patients with diagnosis of infertility increased pregnancy rates.

IS IVF DEHUMANISING? FRENCH BIOETHICS, PATIENTS AND THE LABORATORY

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Problem statement: French bioethics assumes that In Vitro Fertilization (IVF) bears a danger of dehumanizing embryos. Biological science objectifies embryos by selecting them based on morphological quality, when patients project the birth of their child, a subject of humanity. This philosophical duality of object and subject has deep roots into French and European culture: Cartesian philosophy, Christianity and the very birth of bioethics after the Second World War. Yet, nothing is known of the daily laboratory practices in Assisted Reproductive Technology's (ARTs) units. What does a sociological study of ARTs laboratory reveal about bioethics, science and humanization in IVF practices? ***Methods:*** Using a qualitative method, precise empirical data were collected in a French public hospital and a private Indian Clinique. Bioethical debates and subsequent laws were analyzed through precise reading of transcriptions, publications, and media representation. Laboratory practices were documented through in situ observations as well as extensive interviews with embryologists, gynecologists, psychologists and lab technicians. Cross cultural analysis of laboratories was used to highlight scientific similarities of developmental biology in two significantly different countries and the sociocultural milieu were biotechniques are implemented. ***Results:*** French ARTs professionals are aware of local bioethical debates. They also personally do not believe that embryos are cells only, but have a special status based on parental projects. They mingle different representations while performing their science, hybridizing cell quality assessment with potential personhood and family making horizons. When interacting with patients, they also consider the ethical risks of over-objectifying and over-humanizing embryos. They do so in a way that values both scientific evidence and parental projects. ***Conclusion:*** The assumption that IVF and embryo selection constitute a threat to humanization is based on philosophical theories more than actual practices. Bioscientific practices are a means to connect different realms such as family making, biology, health care and bioethics. The social sciences hence bring a unique perspective to sensitive debates and societal tensions. They do so by bringing to the fore actual practices more than abstract sociocultural values.

EVALUATION OF ACTIVATED PROTEIN C RESISTANCE IN WOMEN UNDERGOING OVARIAN STIMULATION PRIOR IN-VITRO FERTILIZATION

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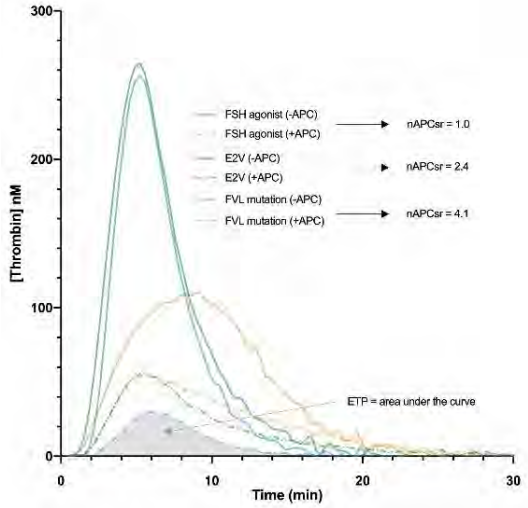
Problem statement: The ovarian stimulation prior in-vitro fertilization causes a significant increase in serum estradiol and progesterone levels which may influence hemostasis. The resistance to activated protein C (APC) is significantly impacted in women using hormonal therapy (e.g., hormone replacement therapy or combined oral contraceptives). The aim of this pilot study was therefore to investigate APC resistance in women undergoing ovarian stimulation, using the validated endogenous thrombin potential (ETP)-based APC resistance assay. ***Method:*** Ten women aged from 29 to 38 were included in this retrospective observational study. Among those women, 3 patients were carrier of a genetic mutation, of which one heterozygous factor V Leiden and two heterozygous prothrombin G20210A mutations. The ovarian stimulation treatment was either menotropin, follitropin, progesterone or estradiol valerate. The ETP-based APC resistance assay is a global coagulation test which aims at assessing the resistance towards APC based on the measurement of thrombin generation over time. Results are expressed in normalized APC sensitivity ratio (nAPCsr) computed as following: [sample ETP (+APC)/sample ETP (-APC)]/[Reference plasma ETP (+APC)/Reference plasma ETP (+APC)]; in which the ETP-parameter corresponds to the area under the thrombin generation curve (Figure 1). The nAPCsr scales from 0 to 10. Scores which are closer to 10 show higher resistance to APC and consequently a higher risk of thrombosis. ***Results:*** Ovarian stimulation appeared to have small impact on APC resistance (Figure 1). Indeed, for most samples, nAPCsr was within normal ranges of 0 to 2.08. A resistance to APC, with nAPCsr of 4.1 was expected for the woman carrier of a Factor V Leiden mutation. A slight resistance to APC (nAPCsr of 2.4) was also observed in the patient taking estradiol valerate. In comparison, women treated with oral contraceptives containing ethinylestradiol show nAPCsr ranging from 3.5 to more than 5.0 depending on the associated progestin. ***Conclusion:*** This pilot study showed that ovarian stimulation with FSH agonist (menotropin or follitropin) had small impact on APC resistance. On the other hand, estradiol seemed to induce a slight APC resistance, which has already been observed in women using estradiol-containing products. Nevertheless, further investigations are needed to confirm these results.

Conflicts of interest: *Jonathan Douxfils is CEO and founder of QUALIblood and reports personal fees from Daiichi-Sankyo, Diagnostica Stago, DOASense, Gedeon Richter, Mithra Pharmaceuticals, Norgine, Portola, Roche and Roche Diagnostics, outside the submitted work.*

Figure 1: Thrombin generation curves in absence (continuous line) **and in presence of APC** (dotted lines) **of enrolled women on FSH agonist treatment** (blue), **of the enrolled woman carrier of a heterozygous factor V Leiden mutation** (yellow) **and of the enrolled woman on follitropin and E2V** (green). The area under the curve represents the ETP-parameter.

Abbreviations: APC, activated protein C; ETP, endogenous thrombin potential; E2V, estradiol valerate, FSH, follicle stimulating hormone ; nAPCsr, normalized APC sensitivity ratio



THE EFFECT OF POST-THAW CULTURE DURATION ON IVF OUTCOMES IN SINGLE BLASTOCYST TRANSFER CYCLES.

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Problem statement: There is limited finding about the effect of post-thaw culture duration on IVF outcome. Therefore, the aim of study is to evaluate clinical outcomes including pregnancy, clinical pregnancy, live birth and miscarriage rates after two different duration of thawing protocols. ***Methods:*** 192 infertile patients who were admitted to the IVF center of Izmir Economy University Medical Park Hospital were included in this retrospective study. Patients underwent IVF treatment having 'freeze-all' cycles. Beside, the patients have no previous embryo transfer attempts and with a single blastocyst transfer were selected in FET cycle. Exclusion criteria were patients (i) women ≥40 years old, (ii) having azoospermia, and (iii) PGS. For group 1, only the best grade I one embryo was vitrified on day 3 and the others re-evaluated on day 5 and were vitrified. In group 2, all the embryos directly were cultured through day 5 and vitrified. In group 1, selected one high-quality cleavage-stage embryo was thawed on day 3 and cultured in the prolonged culture (48 h of post-thaw culture) up to day 5. For group 2, only one blastocyst was thawed and cultured in the short culture (2-4 h of post thaw culture) before blastocyst transfer. ***Results:*** There was no significant difference between groups in terms of baseline characteristics. Also, there were no significant differences between blastocyst qualities according to Gardner's classification (defined as Excellent (AA), good (AB BA), fair (BB) and poor (others)) on day 5 between the groups. Both clinical pregnancy rate and live birth (%50 vs %47,5, p=0.48) rate per blastocyst transferred were found similar in the both groups (Table).

Table Variables	Grup1 (n=112)	Grup2 (n=80)	P-value
Pregnancy (%)	81 (%72,3)	50 (%62,5)	0.16
Clin. Pregnancy (%)	68 (%60,7)	45 (%56,3)	0.42
Live birth (%)	56(%50)	38 (%47,5)	0.48
Miscarriage rate (%)	14(%12,5)	7(%8,8)	0.49

Conclusion: In conlusion, these results support that the duration of post-thaw culture does not effect IVF outcomes in single blastocyst transfer cycles.
Abbreviations: IVF: In vitro fertilization; FET: Frozen-thawed embryo transfer; PGS: Preimplantation genetic screen
Disclosure of interest: None Declared

ABOUT A CASE: CHAPELLE SYNDROME

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44-year-old male undergoing follow-up for hypogonadotropic hypogonadism, bilateral gynecomastia, and history of infertility. During the study of this pathology, it was found that the patient had female chromosomal sex, corroborated by karyotype in peripheral blood. For this reason, a genetic study is requested to identify fragments of the Y chromosome. The patient has a normal diploid endowment for the autosomes studied; Likewise, a double dose is identified for all the markers of the X chromosome. These results are compatible with the 46, XX karyotype provided. However, thorough evaluation of markers on the Y chromosome identifies the presence of a portion of the Y chromosome with a single copy. The fragment present in his genome corresponds to a distal portion of the short arm of the Y chromosome, including the SRY gene. The identification of markers corresponding to the Y chromosome in the patient`s genome, together with the 46 XX karyotype, allows corroborating the diagnosis of **Chapelle Syndrome.** Chapelle syndrome is a rare alteration of sexual differentiation that affects 1 / 20,000 men and represents 2% of cases of male infertility. The most frequent phenotype is that of a normal male, with small testes, but it can also present as a male with ambiguous genitalia and even feminization. It presents with testicular atrophy and azoospermia with infertility; occasionally, it is associated with gynecomastia, obesity, or failure of testicular descent. The presence of the SRY gene translocated from the Y chromosome to the short arm of the X leads to testicular differentiation, although the lack of the region of the Y chromosome that regulates the subsequent differentiation of Sertoli cells leads to testicular atrophy. In 10-20% of cases there is no SRY gene, in which case they are accompanied by more severe abnormalities of sexual development. The diagnosis of this syndrome is cytogenetic. The differential diagnosis should be made mainly with Klinefelter syndrome. The treatment consists of the progressive administration of testosterone to avoid the consequences of the hormonal deficit. With adequate hormonal treatment, the prognosis, with the exception of infertility, in adult life is excellent.

SECOND STIMULATION IN THE SAME OVARIAN CYCLE FOR POOR PROGNOSIS PATIENTS UNDERGOING PGT-A: AN OPTION FOR A FULL-PERSONALIZATION OF THEIR TREATMENT

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Problem statement: A second stimulation in the same ovarian cycle (DuoStim) exploits the peculiar dynamics of human folliculogenesis to conduct two oocyte pick-ups in a short timeframe. Several groups successfully adopted this protocol with various regimens, always showing comparable oocyte/embryo competence after both stimulations. DuoStim is indeed one of the most promising unconventional stimulation protocols for the treatment of advanced-maternal-age and/or poor-ovarian-reserve (AMA/POR) women. The high prevalence of chromosomal aneuploidies can be counterbalanced, via DuoStim, by producing more blastocysts in one ovarian cycle. The main objective of this study was to assess whether an immediate second stimulation in the same ovarian cycle for AMA/POR patients obtaining ≤3 blastocysts for preimplantation-genetic-testing-for-aneuploidies (PGT-A) would be more efficient than the conventional workflow. ***Methods:*** Proof-of-concept matched case-control study. All AMA/POR patients obtaining 0 to 3 blastocysts after conventional-stimulation between 2017-2019 were proposed DuoStim. Of them, 143 couples accepted (DuoStim group) and were matched for maternal age, sperm factor, cumulus-oocyte-complexes and blastocysts obtained after the first stimulation to 143 couples who did not accept (conventional group). GnRH-antagonist protocol with recombinant-gonadotrophins and agonist trigger, ICSI, PGT-A, and vitrified-warmed euploid single-blastocyst-transfer(s) were performed. The primary outcome was the cumulative-live-birth-delivery-rate per intention-to-treat (CLBdR per ITT) within 1-year. If not delivering, the conventional group had 1 year to undergo a second conventional-stimulation. ***Results:*** After DuoStim the CLBdR was 24% (N=35/143). In the control group, instead, the CLBdR after the first attempt was 11% (N=15/143). Among the 128 non-pregnant patients, only 12 returned (165±95 days later; drop-out rate=116/128,91%), and 3 delivered. Thus, the 1-year CLBdR was 13% (N=18/143; p=0.01). Notably, 2 women delivered two LBs after DuoStim and 13 patients with a LB have other euploid blastocysts (0 and 2 in the control, respectively). ***Conclusion:*** In AMA/POR women during PGT-A, DuoStim can be envisioned as a rescue strategy suggested in progress to fully-personalize the treatment in case of poor blastocyst yield after a first stimulation. An immediate second stimulation in the same ovarian cycle might indeed prevent the drop-out and further aging between multiple failed attempts.

FERTILITY, FINANCE AND THE ADD-ON CONTROVERSIES

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Problem statement: In the last decade, an increasing number of add-on technologies have been introduced into the IVF cycle. These new technologies have caused controversy within the sector, as there are divergent views about the strength of the evidence base supporting their introduction and the potential for financial conflict of interest. This study explores the reflections of fertility professionals on this topic in order to understand why these technologies are so controversial. ***Design:*** This presentation draws on 28 interviews conducted in two research projects on this topic. Semi-structures interviews were conducted with fertility professionals in the United Kingdom, the United States and the Netherlands. Fertility professionals included embryologists, medical directors, start-up founders and investors. Interviews were transcribed and thematic analysis was conducted in research teams from the University of Cambridge, University College London and the University of Manchester. ***Results:*** The analysis shows that the add-ons debate reflects foundational ideas about the the changing patient-doctor relationship in clinical decision making; the role of the regulator and medical autonomy; the politics of knowledge production; and commercialisation and financialisation of the IVF sector. ***Conclusions:*** Fertility professionals shared a wide variety of rationalisations and reflections on their decisions whether or not to offer IVF add-ons. The add-on discussion touches on core aspects of professional identity and perceived meaning of medical practice. The controversies surrounding this topic reflect broader changes in the organisation of the IVF sector, in which the power relations between patients, doctors, researchers, directors, investors and shareholders are shifting.

FETO-MATERNAL MORBIDITY DERIVED FROM IN VITRO FERTILIZATION (IVF) GESTATIONS COMPARE TO SPONTANEOUS NON-IVF GESTATIONS: A RETROSPECTIVE COHORT STUDY

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Problem statement: to evaluate if IVF-gestations present a higher risk of developing placental insufficiency (PI) and to determine if IVF might be a risk factor ischemic placental disease (IPD). ***Methods:*** We performed a retrospective cohort study in our tertiary-care hospital including 3982 pregnancies that resulted in a live born infant or an intrauterine fetal demise (IUFD) greater than 23 weeks of gestation, during 2019. Primary outcomes were fetal malformations, IPD and its individual components (preeclampsia, placental abruption, intrauterine fetal growth restriction(IUGR) and IUFD duo to PI. As secondary outcome we stratified our analyses by gestational age according to the moment in which PI was diagnosed (preterm T-student and X2 test were used to analyze quantitative and categorical variables respectively. We used regression analyses to estimate risk ratios (RR) and 95% confidence intervals (CIs) results were adjusted by maternal age, parity and type of pregnancy (singleton or multiple). ***Results:*** 247/3982(6.2%) deliveries were conceived with IVF. We found no significant difference between IFV Vs. non-IVF regarding fetal malformations (6.2%Vs.4.6% p0,304). Multiple gestation was by itself a risk factor for malformations, preterm delivery and IPD, when compare to singleton pregnancies, regardless the type of conception. Compared to non-IVF, IVF pregnancies had greater incidence of preterm delivery and developed both preterm and term IPD, after adjustment for confounding factors and when restricting for singleton pregnancies. The risk of IPD was 3.1 times higher (95% CI, 2.1–4.7) in patients who underwent IVF compared with those non-IVF. This risk remains high for each component of IPD. We observed that IVF pregnancies imply a greater risk of pre-eclampsia (aRR 2.8 IC95% (1.6-5.2)), severe pre-eclampsia (aRR 5.2 IC95% (1.9-9.3)) and earlier development of pre-eclampsia (aRR 3,3 IC95% (1.3-5.2)) compared to non-IVF. We found a stronger association between IVF and IPD in preterm pregnancies compared to term pregnancies. ***Conclusion:*** IVF implies a higher risk of IPD and each of its individual components (PE, IUGR, IUFD). Termination of pregnancy occurs two weeks earlier in IVF gestations. The association is stronger in preterm pregnancies.

Placental Insufficiency by type of conception in all pregnancies.

	Total	IVF N= 247	Non-IVF N= 3735	
PLACENTAL INSUFFICIENCY	228 (5,7%)	42 (17%)	186 (5%)	aOR: 3,1 <p0,001 IC95%(2,1-4,7)
Preeclampsia	121 (3%)	24 (9,7%)	97 (2,6%)	aOR 3,3 <p0,001 IC95% (2,0 – 5,5)
IUGR	106 (2,7%)	22 (8,9%)	24 (2,3%)	aOR 3,4 <p0,001 IC95% (2,0-5,5)
Abruptio	29 (0,7%)	12 (4,5%)	17 (0,5%)	aOR 8,7 <p0,001 IC95% (3,6-21,4)
SGA	71 (1,8%)	4 (1,6%)	67 (1,8%)	p=0,853
IUFD	9 (0,2%)	2 (0,8%)	7 (0,2%)	p= 0,114

DIAGNOSTIC PROCEDURES

OFFICE ENDOMETRIAL SAMPLING – ENDOSAMPLER® RESULTS

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Problem statement: Endometrial sampling is useful in diagnosis of endometrial pathology. It can be performed by office biopsy, hysteroscopic biopsy, or dilatation and curettage1. Often, limited tissue is available and in 5-10% of cases the material collected is insufficient for diagnosis 1,2,3. Regarding office endometrial biopsy, different devices have been developed, usually described as having the same effectiveness. Although, Dijkhuizen et al. found better results for Pipelle, especially in postmenopausal women. 2. The present study pretend to analyze the results obtained for Endosampler® device as an endometrial sampling. ***Methods:*** A retrospective analysis of women submitted to Endosampler® endometrial sampling in our hospital from February 2021-September 2021 was performed. ***Results:*** 55 processes were selected, 54.5% corresponded to postmenopausal women. Median age was 57 (IQR 50,0-68,0) years. Endometrial sampling indications were: abnormal uterine bleeding (AUB), follow-up of endometrial hyperplasia (EH), cervical cytology result of AGC-endometrial and suspicious endometrial thickening on transvaginal ultrasound. No statistical differences were found between indications for biopsy and unsatisfactory results or histologic diagnosis. At 33% of cases, the sample was insufficient for diagnosis, being more frequently in post-menopausal women, although without statistical significance (p=0,09). The most frequent histologic result was “benignfindings” associated with dysfunctional bleeding, in almost 42%. No statistical differences were found in histologic results between pre- and postmenopausal women. In our sample, two cases of endometrial neoplasia were found, both in postmenopausal women with AUB. Thirteen cases of EH were identified in biopsy, five and eight cases on post and pre-menopausal women, respectively. In thirteen cases, a definitive histological result was available. Relatively to agreement of results, two cases of neoplasia weren’t detected on biopsy and five cases of EH in biopsy weren’t confirmed at surgery. ***Conclusion:*** Office endometrial sampling is performed blindly, making it not suitable for focal pathology. Furthermore, unsatisfactory results appear relatively frequently, making it necessary to carry out other auxiliary diagnostic methods. In our study, the prevalence of insufficient sample was higher than usually described. Furthermore, it was more common in postmenopausal women, which may be explained by the smaller sample collected. In conclusion, a larger sample size is necessary in order to validate these results.

DIFFERENCES IN PRENATAL DETECTION OF BIRTH DEFECTS BETWEEN SINGLETONS AND MULTIPLES: AN OBSERVATIONAL STUDY OF MORE THAN 1.9 MILLION BIRTHS IN ZHEJIANG PROVINCE, EASTERN CHINA, DURING 2012-2018

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Objectives: We aimed to compare the differences in prenatal diagnose of BDs between singletons and multiples. ***Method:*** Data were obtained from BDs surveillance system in Zhejiang province from 2012 to 2018. It covers all the births (live births and fetal death ≥28 weeks) born in 90 hospitals located in 30 regions. Births with BDs were followed up within 7 days after delivery. In the study, differences in prenatal detection between singletons and multiples were tested using chi-square test, and multivariate logistic regression models in consideration of confounders. The study included 25 BDs subtypes according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision. ***Results:*** 1.60%(30,325/1,900,166)births were multiples during the study period. The total number of singletons and multiples with BDs were 49,872 and 3,324, respectively. 14.38% BDs in multiples were prenatally detected, being significantly lower than singletons (32.00%, chi2 = 452.94, P0.001). After adjusting for time, maternal age and education, multiples with BDs had lower detection rates in total BDs (ORadj = 0.36, 95%CI: 0.32-0.40), congenital heart defects (OR adj = 0.32, 95%CI: 0.27-0.38), congenital hydrocephalus (OR adj = 0.24, 95%CI: 0.13-0.45), cleft lip with cleft palate (OR adj = 0.18, 95%CI: 0.11-0.30), congenital talipese quinovarus (OR adj = 0.50, 95%CI: 0.27-0.92), cleft lip without cleft palate (OR adj = 0.27, 95%CI: 0.14-0.50), limb reduction defects (OR = 0.33 adj, 95%CI: 0.16-0.68), congenital diaphragmatic hernia (OR = 0.18 adj, 95%CI: 0.06-0.58), trisomy 21 syndrome (OR adj = 0.09, 95%CI: 0.04-0.23), congenital malformation of urinary system (OR adj = 0.30, 95%CI: 0.19-0.47), other chromosomal malformations (OR adj = 0.22, 95%CI: 0.06-0.86) compared to singletons with BDs. Singletons were more easily detected before 28 gestational weeks (74.82% Vs 70.08%). 73.45% BDs were detected by ultrasound, 30.02% by clinical presentation, 4.86% by chromosomal testing. ***Conclusions:*** Singletons with BDs are easily to be detected prenatally and earlier than multiples, particularly in CHD, chromosomal malformations and body surface malformations. Ultrasound is the most frequently used method.

Disclosure: No potential conflict of interests to declare.
Keywords: Prenatal detection, Birth defects, Singleton, Multiple

PREDICTING TUBAL OCCLUSION: DETECTION OF HYSTEROSCOPIC FLUID IN THE POUCH OF DOUGLAS. A PROSPECTIVE COHORT STUDY

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Problem statement: The evaluation of the uterine cavity is important in counseling subfertile female patients and diagnostic hysteroscopy is considered the gold standard tool. There are a number of hysteroscopic techniques for fallopian tube patency testing having been published over the last few years. One of these is a vaginal-sonographic method that detects shifts in the hysteroscopic fluid in the pouch of Douglas before and after diagnostic hysteroscopy. The aim of this study was to determine whether a change in the aforementioned fluid in the pouch of Douglas would be predictive of tubal patency. ***Methods:*** We included 115

subfertile women in a prospective clinical cohort study. All of them underwent surgical fertility evaluation consisting of hysteroscopy and laparoscopic chromopertubation at the Medical University of Vienna. The primary outcome was evaluating whether an increase in the hysteroscopic fluid in the pouch of Douglas would be suggestive of uni- or bilateral tubal patency. A vaginal sonography before and after hysteroscopy was performed, directly followed by laparoscopy with chromopertubation. ***Results:*** Bilateral tube occlusion was detected in 28 women (24.3%) by laparoscopic chromopertubation. 27/40 patients (67.5%) without a hysteroscopic fluid shift showed a bilateral tubal occlusion during the consecutive laparoscopic chromopertubation (p 0.001). 1/75 patients (1.3%) showed a hysteroscopic fluid shift and had bilateral occlusion in laparoscopic chromopertubation (sensitivity of a present fluid shift for uni- or bilateral patency 85.1%, 95% CI: 81.7-99.9, specificity: 96.4%, 95% CI: 75.8-91.8). An increased risk for a false abnormal result – no hysteroscopic fluid shift in case of uni- or bilateral tubal patency – was given when intracavitary abnormalities (odds ratio, OR, 0.038; p = 0.030) and adhesions covering at least one tube (OR 0.076; p = 0.041) were present. ***Conclusion:*** If there is no hysteroscopic fluid shift, our method is a sensitive test for tubal occlusion and the patient should be sent to further testing. However, if there is an increase in fluid in the pouch of Douglas after hysteroscopy, this is sensitive and specific for uni- or bilateral tubal patency.

HYSTEROSCOPIC ASSESSMENT OF TUBAL PATENCY: A RANDOMIZED COMPARISON BETWEEN THE FLOW AND PARRYSCOPE TECHNIQUES

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Problem statement: In counseling subfertile female patients, the evaluation of the uterine cavity is an important issue. Diagnostic hysteroscopy is considered the gold standard tool. Although laparoscopic chromopertubation is the gold standard tool for tubal patency testing, there are also a number of hysteroscopic techniques for the evaluation of fallopian tube patency. For example, the “Parryscope”-technique and the “flow”-technique. In the first mentioned, it is observed whether air bubbles traverse through the tubal ostia, whereas in the “flow”-technique a swirl or endometrial structures are detected. The aim of this study was to evaluate the accuracy of these two techniques for hysteroscopic assessment of tubal patency. ***Methods:*** We included 60 patients suffering from subfertility in our prospective randomized clinical trial. All of them underwent surgical fertility evaluation consisting of hysteroscopy and laparoscopy at the Clinical Division of Gynecological Endocrinology and Reproductive Medicine at the Medical University of Vienna. Hysteroscopy was performed and either the “Parryscope”- or the “flow”-technique was performed for tubal assessment, before laparoscopic chromopertubation was conducted. The primary outcome was the accuracy of these two techniques in comparison to the gold standard of laparoscopic chromopertubation. ***Results:*** The prediction of tubal patency was possible in both study groups (p 0.05), but the “Parryscope”-technique could achieve a higher sensitivity (90.6%, 95% CI: 61.7-98.4) and specificity (100%, 95% CI: 90.0-100.0) than the “flow”-technique (sensitivity: 73.7%, 95% CI: 48.8-90.9 and specificity: 70.7%, 95% CI: 54.5-83.9). ***Conclusion:*** Surgeons can gather additional information from using the “Parryscope”-technique during hysteroscopy. This technique is more accurate in predicting tubal occlusion than the “flow”-technique.

CORRELATION BETWEEN ACTIVATED PROTEIN C RESISTANCE AND THE RELATIVE RISK OF VENOUS THROMBOEMBOLISM IN WOMEN USING HORMONAL THERAPY

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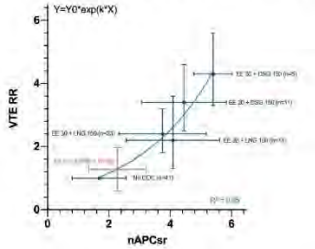
Problem statement: The use of estrogens, alone or associated with progestins, is frequent throughout a woman’s life, but exposes to an increased risk of venous thromboembolism (VTE). Identifying one or several biomarkers to dress the “coagulability status” of patients before et during the course of hormonal therapy would be an interesting approach to minimize the thrombotic risk. Activated protein C (APC) resistance could be a potential candidate as it is significantly impacted by the use of combined oral contraceptives (COC) and hormone replacement therapy. The aim of this study was therefore to assess the VTE risk prediction capacities of the normalized APC sensitivity ratio (nAPCsr), the score frequently used to express APC resistance. ***Method:*** An in silico-modeling was computed by combining both the nAPCsr for specific COC preparations with their respective VTE relative risk issued from the Cochrane network meta-analysis of de Bastos (comparing multiple treatment simultaneously in a single analysis). From this metanalysis, 14 studies compared different types of COCs versus non-users. nAPCsr values were obtained retrospectively from 139 women’s samples of which 41 were non-users, 15 were using ethinylestradiol 20 µg/levonorgestrel 100 µg, 33 were using ethinylestradiol 30 µg/levonorgestrel 150 µg, 11 were using ethinylestradiol 20 µg/desogestrel 150 µg, 5 were using ethinylestradiol 30 µg/desogestrel 150 µg and 34 were using the novel combination estetrol 15mg/drospirenone 3 mg. ***Results:*** As shown in figure 1, an exponential growth equation was used to draw the correlation between nAPCsr and the relative risk of VTE depending on the type of COC. Out of 34 women using the new combination estetrol/drospirenone, the mean nAPCsr was 2.28. By interpolation, this new association might express a relative risk of 1.29. This is in line with data obtained so far in which estetrol associated with drospirenone shows a promising hemostatic profile compared to the other COCs. ***Conclusion:*** Caution is required when interpreting these data since this prediction model is only exploratory and further investigations and validation are needed. However, these data support the idea that the nAPCsr could become a universal test to assess the hormone-induced risk of VTE in women during their entire lifetime.

Conflicts of interest: Jean-Michel Foidart is a member of the board at Mithra Pharmaceuticals. Jonathan Douxfils is CEO and founder of QUALIblood and reports personal fees from Daiichi-Sankyo, Diagnostica Stago, DOASense, Gedeon Richter, Mithra Pharmaceuticals, Norgine, Portola, Roche and Roche Diagnostics, outside the submitted work.

Figure 1: Correlation between normalized APC sensitivity ratio (nAPCsr) and relative risk (RR) of venous thromboembolism (VTE) (de Bastos, 2014) depending on the type of combined oral contraceptives (COC) (i.e., ethinylestradiol (EE) 20 µg/levonorgestrel (LNG) 100 µg; EE 30 µg/LNG 150 µg; EE 20 µg/desogestrel (DSG) 150 µg; EE 30 µg/DSG 150 µg). Non-user group used as a reference (VTE RR = 1) showed a mean nAPCsr ± standard deviation of 1.68 ± 0.88 (n = 41). EE 20/ LNG 100 showed a mean nAPCsr ± standard deviation of 4.09 ± 1.53 (n = 15) and VTE RR (CI 95%) of 2.2 (1.3–3.6); EE 30/LNG 150 showed a mean nAPCsr ± standard deviation of 3.75 ± 1.43 (n = 33) and VTE RR (CI 95%) of 2.4 (1.8–3.2); EE 20/DSG 150 showed a mean nAPCsr ± standard deviation of 4.45 ± 1.38 (n = 11) and VTE RR (CI 95%) of 3.4 (2.5–4.6); EE 30/DSG 150 showed a mean nAPCsr ± standard deviation of 5.40 ± 0.63 (n = 5) and VTE RR (CI 95%) of 4.3 (3.3–5.6). New combination E4/DRSP showed a nAPCsr of 2.28 and an intrapolated VTE RR (CI 95%) of 1.29 (0.62–1.97).



COMPARISON OF FROZEN SECTION WITH PARAFFIN BLOCK PATHOLOGICAL EXAMINATION RESULTS IN PATIENTS WITH GYNECOLOGICAL MALIGNANCIES AT PROF. DR. R.D. KANDOU GENERAL HOSPITAL

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Problem statement: Gynecological malignancy remains a major health problem in women. Paraffin block pathological examination is considered as the gold standard for detecting gynecological malignancies. Another alternative pathologic examination tool, frozen section / vries coupe (VC), can also be performed for faster results. A study conducted by Arnila R, et. al. (2019) at Dr. Mohammad Hospital Palembang showed that frozen section examination was accurate enough to differentiate malignant ovarian tumors, but not many studies have been conducted, specifically in Indonesia, to compare frozen section examination with paraffin block in terms of accuracy, sensitivity, and specificity. The aim of our study is to compare between frozen section and paraffin block examination results in patients with gynecological malignancies at Prof. Dr. R.D. Kandou General Hospital in 2020. ***Method:*** This research was a descriptive analytic study. The number of study samples was 37 samples consisting of patients with gynecological malignancies at Prof. Dr. R.D. Kandou General Hospital within the period of January to December 2020. The data was collected and then analyzed using Microsoft Excel software. ***Results:*** Based on the data obtained from 37 patients with gynecologic malignancies, which includes ovarian, cervical, and uterine malignancies; 28 patients (75% cases) showed similar results on frozen section and paraffin block examinations, while 9 patients (25% cases) showed different results on the frozen section and paraffin block examinations. ***Conclusion:*** There was no significant difference between the results of frozen section and paraffin block examination in detecting gynecologic malignancies at Prof Dr. R.D. Kandou Hospital Manado within the period January to December 2020

Keywords: Frozen Section, Paraffin Block, Gynecological Malignancy
Disclosure of interest: The authors would like to acknowledge the support from doctors, and paramedics of The Obstetrics and Gynecology Department, Faculty of Medicine Sam Ratulangi University - Prof. R. D. Kandou General Hospital Manado. All authors were involved in the conception of the manuscript, editing of the manuscript, and in the clinical care of the patient. The authors declare that data supporting the findings of this study are available within the article. There are no financial disclosure and conflict of interest to declare.

ARBOTEST - SELF-MADE TEST FOR DETECTING RUPTURE OF MEMBRANE

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Problem statement: Premature rupture of membrane can cause several com plications in pregnancy. By detecting leakage of amniotic fluid consecutive inflammation and severe outcomes can be prevented. Arborisation test is well-know feasible method for detecting rupture of the membrane. Vaginal smear containing amniotic fluid will show arborisation due to its sodium chloride contain, assessed by microscope used 40X magnification. ***Methods:*** Using the equipment and application on a smartphone, patients can do the sampling for themself at home. The microscopic image of the slide is sent for a server by the application, that will give a result of positiveness or negativeness. The algorithm has been trained previously by images and using deep neural network based methods, it can evaluate the test photos. ***Results:*** Photos of magnified image of vaginal smear were divided into positive and negative group by a gynecologist (1270 images, 662 negative, 608 positive). The pre-trained model assessed all the images. The accuracy of the method was 98.58% with sensitivity of 97.36, specificity of 99.69, negative predictive value of 97.63 and positive predictive value 99.66. ***Conclusion:*** In modern ages and in the ages of pandemic telemedicine could decrease the number of patient-doctor meeting. By using Arbotest, complications of premature rupture of membrane can be detected earlier and could be prevented more severe complications.

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FETOMATERNAL MEDICINE

PREECLAMPSIA AND FETAL CONGENITAL HEART DEFECTS – SHOULD WE ROUTINELY SCREEN?

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Problem statement: To compare populations with isolated preeclampsia (PE) and PE complicated with fetal congenital heart defects (CHD). ***Methods:*** Retrospective study including all singleton pregnancies complicated with PE admitted to a tertiary center between 2018-2020. Multiple gestations were excluded from our cohort. We sought for perinatal CHD at three moments: antenatally (fetal ultrasound); through cardiac examination at birth; and postnatally, by looking for pediatrics' cardiology appointments into infants' files. If no cardiac abnormalities were identified at least six months postpartum, CHD were excluded. Two groups were then considered: PE both with (G1) and without (G2) fetal/newborn's CHD. A descriptive analysis and parametric tests were performed. Statistical significance considered was p0,05. ***Results:*** Out of 173 pregnant women with PE, 164 met the inclusion criteria, 13 and 151 cases in G1 and G2, respectively. Prevalence of CHD was 7,9%, declining to 5.5% if we exclude 4 cases of patent foramen ovale (PFO) diagnosed before 2 years-old. Septal defects, PFO after 2 years-old, dilation of cardiac chambers and aortic isthmus narrowing were the main CHDs observed. Comparing groups of PE, both mean maternal age (35,5 years in G1 and 32,5 years in G2, p=0,08) and rate of assisted reproductive technology (15.4% in G1 and 3.3% in G2, p=0,09) were higher if CHDs were diagnosed. In G1, diagnosis of PE was made one week earlier (32 vs 33 weeks) and increased rates of early PE, i.e. before 34 weeks, were found (46,2% vs 34,4%). However, PE in prior gestation or history of chronic hypertension was more frequent in PE without perinatal CHD group. Performance of fetal echocardiograms during

pregnancy was 53,8% in G1 and 44.4% in G2. For neonatal morbidity outcomes (birthweight, NICU admission, duration of hospitalization), we didn't find statistical significance in any of these results. ***Conclusion:*** The prevalence of CHD in PE is increased compared to low-risk pregnancies, which is around 1%. The association between PE and CHD, more evident in early PE, may lead to consider inclusion of routine fetal and neonatal echocardiograms in all women admitted for PE. This strategy could improve early diagnosis and management of newborns with CHD.

PERSISTENT CAESAREAN SCAR PREGNANCY: A CASE REPORT

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Problem statement: Caesarean scar pregnancy (CSP) is a late complication of caesarean section. Its incidence has increased worldwide in recent years due to the increasing number of caesarean deliveries and the advances in imaging. An early diagnosis and prompt management and follow up are essential to avoid catastrophic complications, such as bleeding and uterine rupture that can end in a hysterectomy. Currently there is no consensus on the best management for CSP, and various surgical, medical, and minimally invasive therapies have been described. ***Methods:*** This is a case report, whose aim is to present the importance of recognising and managing properly a caesarean scar pregnancy. Results: A 35-year-old woman, G4P2 (2 caesarean sections 11 and 18 years prior), with history of depression and anxiety, presented herself at a family planning appointment requesting an intrauterine system (IUS) placement one week after a uterine aspiration of a CSP, in the context of a voluntary interruption of pregnancy at 8 week's gestation. A serum HCG concentration measurement was requested, presenting a value of 672 mUI/mL three weeks after the aspiration. A transvaginal ultrasound was performed revealing a vascularized heterogeneous mass implanted on the caesarean scar measuring 19x15x16mm, with no other relevant abnormalities. A persistent CSP was diagnosed and after a review of the literature the patient was given 90mg of intramuscular methotrexate. The follow up with serial serum HCG concentration measurements showed a gradual decrease until normalisation one month after the injection. The transvaginal ultrasound performed 4 months after the injection showed no abnormalities and an IUS was inserted with no complications. ***Conclusion:*** CSP is an important complication of caesarean section that needs to have a careful approach due to its risks and possible complications. Because this case was initially approached as an interruption of pregnancy and not an ectopic pregnancy implanted on a caesarean scar, the correct follow up was not put in place. The gold standard management is not defined yet, making it necessary to carry out high-quality, large-sample, longer follow-up trials to reach more definitive conclusions and create guidelines.

REPEATED VAGINAL DELIVERY IN WOMAN WITH UNCORRECTED TETRALOGY OF FALLOT (TOF) AND MAJOR AORTO-PULMONARY COLLATERAL ARTERIES (MAPCAs): A CASE REPORT

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Problem statement: Pregnancy with uncorrected Tetralogy of Fallot (TOF) is associated with elevated risk of maternal morbidity and mortality related to worsening cardiac function to accommodate the physiological hemodynamic changes in pregnancy. Management of pregnancy with uncorrected TOF has always been a challenge and require case-by-case analysis to optimize pregnancy outcome. ***Method:*** We present a rare case of a 21-year-old secundigravida, with an uncorrected TOF, major aorto-pulmonary collateral arteries (MAPCAs), and history of successful vacuum-assisted vaginal delivery in previous pregnancy. She was seen for the first time at the Ob/Gyn outpatient clinic of Dr. Sardjito Hospital at 6 weeks of gestational age (GA). We immediately arranged a multidisciplinary clinical conference to assist her pregnancy, co-managed with cardiologist and anesthesiologist. The pregnancy was carefully monitored, she was planned to have fetal screening at 20-22 weeks of GA, earlier lung maturation at 26-28 weeks of GA, and delivery at 32 weeks of GA. Overall, the pregnancy proceeded smoothly, she tolerated the pregnancy quite well without any specific medication. Upon admission for delivery, the patient was stable, no chest pain and no shortness of breath was observed, her heart rate (HR) was 78 beats/min, oxygen saturation (SpO2) was 82-92%, and hematocrit was 46.8%. A murmur was clearly heard at her left 3rd intercostal region along the parasternal border. The ultrasound examination showing single fetus, longitudinal lie, cephalic presentation, and estimated fetal weight of 1596 grams. She was managed with a vacuum assisted vaginal delivery with Misoprostol for labor induction at Intensive Care Unit (ICU), supported by Epidural Labor Analgesia (ELA). ***Result:*** After 16 hours, a female baby was born by a vacuum-assisted vaginal delivery, with body weight 1478 grams and Apgar score 7/8. Intrauterine Contraception Device was chosen as contraception and was placed immediately after delivery. She was discharged 3 days afterwards. ***Conclusion:*** Careful monitoring and multidisciplinary team involving an obstetrician, especially maternal-fetal medicine sub-specialist, cardiologist, anesthesiologist may improve the outcomes in women with uncorrected TOF. Furthermore, expert care should be followed by scrupulous counseling regarding any possible maternal and neonatal outcome.

COVID-19 PANDEMIC AND ITS IMPACT ON PERINATAL OUTCOMES BETWEEN SYMPTOMATIC AND ASYMPTOMATIC WOMEN

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Introduction: Coronavirus disease 2019 (Covid-19) has been increasing among pregnant women worldwide. Its impact on maternal, fetal and neonatal health is still scarce in the published literature. As routine Covid-19 prenatal screening has been established for all women requiring hospitalization, it is not clear whether symptomatic women carry worse pregnancy outcomes than those without symptoms. We aimed to analyze perinatal outcomes between symptomatic and asymptomatic women admitted to our center. ***Materials and Methods:*** A single center study was carried out for fourteen months. All pregnant women with confirmed Covid-19 infection were enrolled and their perinatal outcomes were analyzed in two groups based on whether they were symptomatic or not. The primary outcomes were composite adverse fetal, neonatal, and maternal outcomes and their comparison between study groups. ***Results:*** Out of 209 tested Covid-19 positive women, 62 (30%) presented with one or more infection related symptoms. Symptomatic women were older, multiparous, carried ≥ 1 comorbid condition and attain infection at earlier gestational age (44% vs 28%), (82% vs 69%), (28% vs 16%) and (34 vs 36 weeks) (p0.05), when compared to asymptomatic study group respectively. Maternal composite adverse outcomes were higher in symptomatic group and showed either one or more outcomes: positive chest radiological findings, requiring

hospitalization with oxygen supplementation or maternal death (8% vs 0.7%) (p0.05). Composite fetal and neonatal adverse outcomes: miscarriage, fetal or neonatal death, admission to neonatal intensive care unit and neonatal Covid-19 infection were not statistically significant (p 0.05) between symptomatic and asymptomatic women. ***Conclusion:*** Covid-19 infection among symptomatic pregnant women may carry higher risk for adverse maternal outcomes. It may be associated with their advanced age and comorbid conditions. Maternal infection associated symptoms per se, likely do not pose an increased risk for adverse fetal or neonatal outcomes.

MATERNAL-FETAL OUTCOMES IN OBESE WOMEN – 2 YEARS EXPERIENCE

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Problem statement: Obesity is a major public health concern and its prevalence in reproductive-age women has been rapidly increasing over the past few decades. Obesity can be classified in three types – table 1.

	Body Mass Index (BMI) kg/m2
Type I	30-34,99
Type II (severe obesity)	35-39,99
Type III (morbid obesity)	over 40

Table 1: Obese pregnant women are at increased risk of developing major maternal and perinatal complications such as gestational diabetes (GD), hypertensive disorders of pregnancy (HDP) including pre-eclampsia (PE). Also, the need of labour induction and dystocic deliveries are higher among these women. ***Methods:*** Retrospective descriptive study based on the analysis of data of pregnant women with type III obesity, who attended to at least one high-risk pregnancy appointment at the Professor Doutor Fernando Fonseca Hospital (Portugal, Lisbon) in the last two years (2019-2020). Statistical analysis through Microsoft Excel©. ***Results:*** In this period, there were 156 cases of type III obese pregnant women whose average age was 31 years old (19-46). Regarding personal history, 18,6% had chronic hypertension and 1,9% were diabetic. Mean BMI at 1st trimester was 44,3 (40,2-58,5) and 44,9 at 3rd trimester (40-71,5). Concerning pregnancy complications, there were 43 cases of GD (27,7%), 22 cases of HDP (14,2%) and 18 of PE (13,5%). The prevalence of these complications was higher with increasing BMI, particularly for HDP. Mean gestational age at delivery was 39,3 weeks, with 12 preterm deliveries (8%) and 1 stillbirth at 35 weeks gestation. Eutocic delivery occurred in 59 cases (39,6%) and CST delivery in 72 (48,3%), 18 of which due to induction failure (25%) and 5 due to suspected macrossomia (6,9%). 15 newborns (11%) were considered large for gestational age (LGA), of whom 8 (53,3%) were born to mothers with GD. Among LGA newborns, there was 1 case of shoulder dystocia (6,7%) and 2 cases of neonatal hypoglicemia (13,3%). ***Conclusion:*** The results of our study reflect the ones found in the literature. It is, however, important to highlight the importance of a multidisciplinary approach to prevent the excessive weight gain in this population in order to prevent poor obstetric outcomes.

WHEN PREGNANCY DELAYS CANCER DIAGNOSIS: A CASE REPORT

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Problem statement: Cancers diagnosed during pregnancy and in the immediate post partum period are only seen in one in 1000 women, however frequency might increase due to the trends in delayed childbearing. The main reason for this is that many early signs of cancer can mimic pregnancy symptoms and so fail to get aggressively investigated as they would in the non pregnant woman. ***Methods:*** The case we present is of a previously healthy 33 year old woman in her second pregnancy. Note was made of a slight microcytic anaemia at booking but this was presumed to be due to her condition and in fact improved with iron supplements. The course of the pregnancy was uneventful until around 36 weeks when her blood pressure rose and blood tests including a liver profile were organised. These were deranged and since the bile acid levels were also slightly elevated the patient was suspected to have early pre-eclampsia or cholestasis and was induced and delivered at 38 weeks. On presenting for her post natal visit six weeks after, she was complaining of vague symptoms including loss of appetite and fatigue and since her liver profile was still deranged she was admitted for further investigations. ***Results:*** Imaging revealed a large mass in her colon already spreading to her lymph nodes and liver and causing ascites. Primary debulking surgery was carried out seven weeks post partum and a transverse colon tumour was excised at hemicolectomy. The plan after this was to deliver chemotherapy with regular imaging to monitor progress. The patient was undergoing her third cycle at the time of writing. ***Conclusion:*** This tragic case demonstrates the pitfalls in diagnosing cancer during pregnancy. Both the patients and the medical team themselves can easily blame the pregnancy for many of the telltale symptoms of malignancy which would definitely not go unnoticed outside of this period. A high index of suspicion is needed when interpreting tests taken during pregnancy as this might help with earlier detection of certain cancers and hence earlier resort to treatment and eventually better prognosis.

ADVANCED MATERNAL AGE: A CROSS-SECTIONAL STUDY IN A TERCIARY CARE CENTER

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Problem statement: Pregnancy in older women has become more prevalent over the last few decades due to socioeconomical factors and advances in fertility care. Advanced maternal age (AMA) is classically defined as pregnancy in women over 35 years at due date, although some studies refer it as over 40 years old. However, it is considered a risk factor for many maternal and perinatal adverse outcomes. ***Methods:*** Retrospective descriptive study based on the analysis of data of pregnant women who gave birth in the first trimester of 2021 at the Professor Doutor Fernando Fonseca Hospital (Lisbon, Portugal). Statistical analysis through MicrosoftExcel©. ***Results:*** AMA women constituted 253 (25.3%) of the total deliveries in this period, with a mean age of 38. There were identified 8 *in vitro* fertilization (IVF) and 5 twin pregnancies.Regarding obstetric history, 38% had history of miscarriage and 17.8% were nulliparous. Concerning pregnancy complications, there were 49 cases (19.4%) of diabetes during pregnancy and an incidence of 14.2% of Hypertensive Disorders of Pregnancy (HDP), including 17 cases (6.7%) of PE/HELLP syndrome and 20 cases (7.9%) of chronic arterial hypertension. There were 3 cases (1.2%) of placenta previa and 5 cases (2%) of placental abruption.Perinatal outcomes included 34 (13.4%) preterm deliveries, with 35 (13.8%) light for gestational age newborns, 5 fetal deaths and 3

neonatal deaths. More than half (54.2%) had access to some kind of prenatal screening test, but merely 47 women were submitted to amniocentesis. There were 2 births with Down syndrome, both with prenatal diagnosis, 8 cases (3,2%) of congenital abnormalities, 50% of those being cardiac defects.The caesarian section rate (49%) was found to be higher in AMA than global rate (38.5%). Labor was induced in 72 (28.5%) cases. ***Conclusion:*** The incidence of AMA pregnancies is rising consistently over the years, representing in our center more than a quarter of all births in this first semester. Our results are consistent with the ones found in the literature. Although AMA is a known poor prognostic factor in pregnancy and perinatal outcomes, there remains no consensus opinion for the management of pregnancy in this particular risk group.

POST-PARTUM OVARIAN VEIN THROMBOSIS COMPLICATED WITH PULMONARY EMBOLISM AND INFECTION

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Problem Statement*:* Ovarian vein thrombosis (OVT) is a rare condition that can occur during puerperium, with higher incidence after cesarean sections. Attempted diagnosis and treatment are crucial, since when left untreated OVT may progress for inferior vena cava resulting in pulmonary embolism (PE) and sepsis. This report describes a case of postpartum OVT, which complicated with Pulmonary infarction with subsequent infection in a woman without known major risk factors. ***Methods:*** Case report and literature review. ***Results:*** A 30-year-old healthy woman was admitted to hospital with dyspnea and pleuritic chest pain 5 days after an uncomplicated cesarean section, performed due to breech presentation. Upon admission she was febrile and tachycardiac and blood tests revealed elevated inflammatory markers and D-dimers. A CT pulmonary angiography was performed revealing an inferior right lobe segmental embolism with a concomitant consolidation area and a homolateral 15 mm pleural effusion. Assuming the diagnosis of PE, we initiated therapeutic anticoagulation with low-molecular-weight heparin (LMWH). The patient progressed with fever and elevation of inflammatory markers. Therefore, to search for a pelvic septic thrombosis, an abdominal-pelvic CT-Scan was performed and showed right ovarian vein thrombosis. Despite appropriate treatment for pelvic septic vein thrombosis (Ceftriaxone, Metronidazole and LMWH), the patient maintained daily fever peaks and inflammatory markers rise. With suspicion of infection of the pulmonary infarcted area, we changed antibiotics to piperacillin/tazobactam and performed a thoracoscopy with debridement of empyema areas. After that, the clinical evolution was favorable, and the patient was discharged after 21 days of antibiotherapy. The patient continued anticoagulation for 6 months. **Conclusion:** Every woman who is pregnant or in the postpartum period has a higher risk for thrombosis. Even though this patient didn't have any major risk factor for thrombosis, except for post-cesarean section, she presented with a severe venal thrombotic pathology. As the symptoms may be subtle, high clinical suspicion is needed for an accurate diagnosis and prompt initiation of anticoagulation, which is crucial to reduce mortality.

TRANSDUODENAL DRAINAGE OF LARGE PANCREATIC PSEUDOCYST IN PREGNANCY

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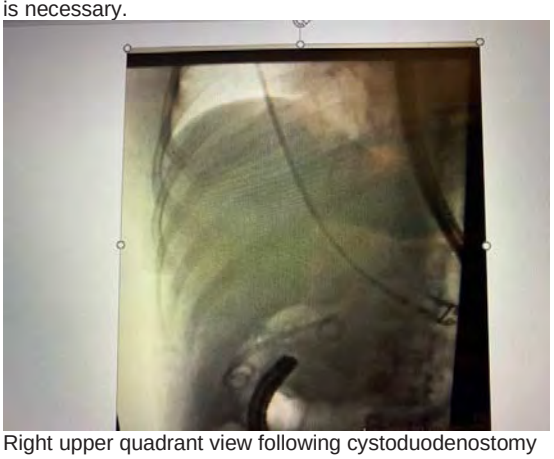
Pancreatitis is a rare morbidity encountered during pregnancy. However, careful management is indicated due to its association with high rates of fetal-maternal mortality. As inflammation damages pancreatic cells, enzyme and fluid leakage can result in pseudocyst formation, a dangerous and life-threatening complication of pancreatic disease if rupture occurs. ***Case report:*** A 32-year-old G5P2022 at 34w1d was evaluated for acute-on-chronic pancreatitis and found to have an enlarged pancreatic pseudocyst measuring 10.5 x 10.5 x 10.4 cm. Prior to pregnancy the cyst measured 4.4 x 5 x 7.3 cm. She had magnetic resonance cholangiopancreatography (MRCP) evaluation and endoscopic ultrasound guided (EUS) aspiration and drainage. Drained fluid was positive for bacteria and the patient was treated with antibiotics. She was readmitted with abdominal pain 35w6d and ultrasound demonstrated a pseudocyst reformation measuring 8.8 x 8.6 cm. She delivered by repeat cesarean section at 37 weeks to allow definitive treatment and stent placement for pancreatic duct (PD) leakage. Two weeks following delivery she was readmitted with a 7.7 x 7.4 cm pseudocyst on the head of the pancreas with no obvious communication to the PD. She had cystoduodenostomy with placement of double-pigtail stents to achieve prolonged drainage. ***Conclusion:*** There are no definitive guidelines instructing the management of large pseudocysts in pregnancy. Conservative management is the recommended treatment modality throughout pregnancy, but symptomatic or enlarging pseudocysts necessitate prompt intervention to prevent rupture. The endoscopic drainage technique is now preferred over more invasive or open surgical approaches depending on pancreatic pseudocyst location and accessibility. Early intervention recommendations in symptomatic cases typically include providing adequate nutritional support and percutaneous drainage (PCD) depending on the severity of symptoms and location of the pseudocyst. Due to the emergence of safer and more efficacious drainage techniques, such as EUS-guided drainage, earlier intervention may be advantageous to reduce the risk of pseudocyst complications later in pregnancy. More research to create adequate prevention and management guidelines for this condition in pregnancy is necessary.



Right upper quadrant view following cystoduodenostomy

HEMODIALYSIS IN PREGNANCY - HOW OFTEN IS TOO OFTEN?

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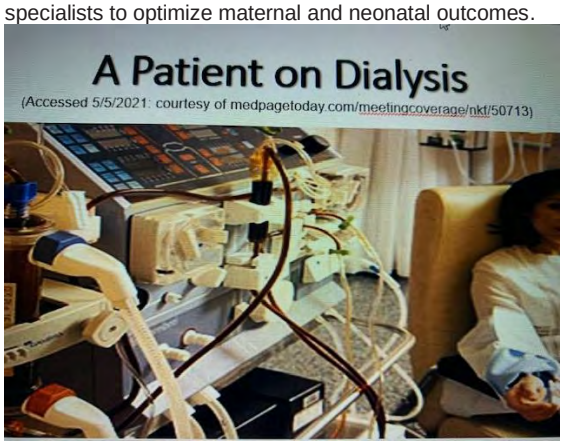
Background: End-stage renal disease (ESRD) is diagnosed when the glomerular filtration rate (GFR)

15ml/min per 1.73 m2 or if the patient requires dialysis (hemodialysis or peritoneal dialysis) with consideration of renal transplantation. Women with ESRD often have infertility, however, when pregnancy occurs, there is increased risk for preeclampsia-eclampsia, preterm delivery, neonatal intensive care unit (NICU) admission among other morbidities with possible fetal or maternal mortality. ***Case:*** A 33-year-old G4P2012 with past medical history of peripartum cardiomyopathy and ESRD requiring hemodialysis (HD) presented to the emergency department for a clotted hemodialysis catheter. She was found to have viable intrauterine pregnancy by 7-week ultrasound. At the onset of pregnancy, the patient was oliguric and undergoing HD treatment three times per week. Blood pressures remained in the severe ranges throughout the pregnancy, requiring multiple antihypertensive medications. Several specialists were involved in her care including maternal-fetla medicine (MFM), cardiology, nephrology, neonatology, and hematology. Her HD sessions were increased to five times per week, totaling 20 hours, by the second trimester. The patient was admitted to the hospital at 25 weeks and 2 days gestation secondary to chronic hypertension with superimposed preeclampsia with severe features. Blood pressures on arrival ranged from 180-200s/100s-110s. The patient required magnesium sulfate for seizure prophylaxis and multiple parenteral antihypertensive medications. Urgent cesarean section was performed at 27 weeks and 3 days of delivery of liveborn female weighing 917g admitted to NICU. In the postpartum period HD treatment was decreased to three times per week. ***Discussion:*** Management of dialysis patients should include preconception/contraceptive counseling to address appropriate medications to use or avoid. If pregnant, ESRD patients require optimization of maternal status including stabilization of blood pressure, keeping BUN 15mg, maternal hemoglobin 10-11g/L, measurement of serum calcium, phosphorus and parathyroid hormones/vitamin D possibly every trimester, and recommended protein of 1.5 to 1.8g/kg per day and taking aspirin for preeclampsia prevention. A treatment goal of 20 hours per week of hemodialysis is also recommended to improve fetal outcomes. Management of pregnant ESRD patients requires a multidisciplinary approach involving several specialists to optimize maternal and neonatal outcomes.



GASTROSCHISIS - ANTENATAL DIAGNOSIS IS CRUCIAL

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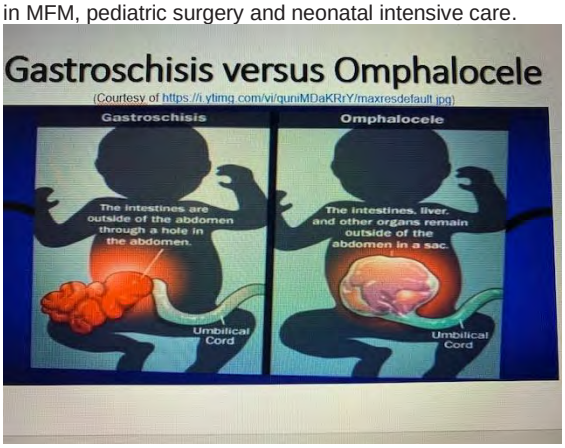
Background: Gastroschisis is herniation of abdominal contents with no sac through the abdominal wall adjacent to the umbilicus. Incidence may range from 2 to 5 per 10,00 live births and the cases are typically discovered during prenatal ultrasound. It is different from omphalocele because omphalocele has membranous sac covering whereas gastroshisis does not have membranous covering. ***Case report:*** A 22 year old G3P1011 at 15 weeks gestation was seen for initial prenatal care. She had a previous normal live birth and a spontaneous abortion at 8 weeks gestation. She had no personal or family history of birth defects. Her ultrasound showed a viable singleton intrauterine pregnancy of appropriate size for gestational age but had gastroschisis present. No other fetal anomalies noted. Antenatal fetal monitoring including growth ultrasound at appropriate intervals between visits confirmed previous findings with appropriate interval growth. Consultation with maternal-fetal medicine (MFM), pediatric surgeon and neonatology team. The patient delivered via urgent cesarean section at 36 weeks and 5 days' gestation due to preterm premature rupture of membranes and reassuring fetal heart trace. The bowel was wrapped in sterile saline dressings and had surgery to repair the defect soon after. Baby was on total parenteral nutrition initially and gradually advanced to formula feeds and finally discharged home in stable condition on postoperative day 39. ***Discussion:*** This case had a benign and stable post-operative course and satisfied parents. Early monitoring during pregnancy allows for planning and making the family aware of possible complications that may arise. It allows for the surgery to take place immediately following delivery to decrease the likelihood of infection and increase the success rate of the procedure. Currently, the repair of gastroschisis can be done as a single primary repair, or if required, can be a step-wise repair if there is difficulty at the time of the initial surgery. Early anetenatal diagnosis of gastroschisis provides opportunity to be ready for emergent surgery immediately following delivery to reduce post-operative complications. It also allows for early antenatal transfer of care to a teritiary medical center with specialists in MFM, pediatric surgery and neonatal intensive care.



A SHORT INTER-PREGNANCY INTERVAL INCREASES OFFSPRING BIRTHWEIGHT. A STUDY OF 764,203 WOMEN WITH A FIRST AND A SECOND SINGLETON DELIVERY IN NORWAY, 1970-2019

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Problem statement: A short inter-pregnancy interval is reported to increase the risk of giving birth to a low birthweight infant, and the World Health Organization (WHO) suggests two-three years inter-pregnancy interval to optimize the child's health. Waiting two-three years before attempting a new pregnancy may seem long for a 35-year-old first time mother who wants more than one child. We aimed to provide updated information about the relation of inter-pregnancy interval with birthweight of the second child. ***Methods:*** We performed a follow-up study from the

first to the second delivery by using data from the Medical Birth Registry of Norway. We included all women with two singleton deliveries at gestational week 28 or beyond during the years 1970-2019 in Norway, a total of 764,203 women. Our outcome measure was change in mean birthweight from the first to the second delivery. Inter-pregnancy interval was defined as the time from a first delivery to onset of a new pregnancy. ***Results:*** Mean birthweight increased from the first to the second delivery by 151 grams (g), from 3461g to 3612g. The increase was highest in children born after 30 years and 35 years at first delivery. In women with a first stillborn child, mean birthweight increased by 984g to the second delivery, but we found no relation of birthweight with inter-pregnancy interval. Our results are adjusted for year of first delivery, maternal country of birth, maternal age, new father in second pregnancy, and maternal diabetes or hypertension in first pregnancy. **Conclusion:** We found that offspring birthweight at second delivery was highest if the inter-pregnancy was less than six months. Our results do not discourage a short pregnancy interval.

THROMBOCYTOPENIA AND POSTPARTUM HEMORRHAGE IN A PREGNANT PATIENT WITH COVID-19 INFECTION: A CASE REPORT

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Problem statement: Thrombocytopenia associated with COVID-19 during pregnancy has several important implication such as increasing the bleeding risk of performing invasive procedures. ***Methods:*** We present a case of a pregnant who was admitted by myalgia and fever, tested positive for COVID-19, and was found to have severe thrombocytopenia on routine complete blood count collected at the time of admission. ***Results:*** A 37-year-old, primigravid and referred to emergency room at 32 weeks and 3 days of gestation with myalgia and fever. The routine complete blood count upon admission was hemoglobin 10,7 g/dL and a platelet count of 35 x 109/L (120 ×109/L at second trimester). No changes in liver function tests. She was found to be positive on COVID-19 testing. She initiated dexamethasone 6 mg once daily. In the second day, 35 x 109/L of a platelet count and she felt decreased fetal movements. Fetal heart rate tracing showed variable decelerations and after a prolonged deceleration, it was decided for immediate cesarean delivery. One unit of pooled platelets was administered. In the third day, she had abdominal pain on palpation and decompression. The complete blood count was hemoglobin 5,1 g/dL and a platelet count of 41 x 109/L. Abdominal ultrasound with free fluid in the abdominal cavity. It was done an exploratory laparotomy that showed a huge hemoperitoneum in the left parietocolic groove, and it was not possible to identify the origin. The patient received two units of packed red blood cells and one unit of pooled platelets. In the fourth day, hemoglobin was 8,1 g/dL and a platelet count of 45 x 109/L. Administered immunoglobulin 1g/kg and dexamethasone 8 mg(day. In the fifth day, the patient presented with dyspnea and the computed tomography chest showed a focus of condensation with ground-glass density compatible with pneumonia caused by COVID-19. She started noninvasive ventilation with Helmet. She continued to improve clinically and was discharged home on day 13. At the time of discharge, the patient's platelet count was 64x109/L. ***Conclusion:*** A rapid recognition of severe thrombocytopenia, if present in mildly symptomatic patients with COVID-19, is crucial for delivery of safe.

ACUTE HEPATITIS IN A PREGNANT PATIENT WITH COVID-19 INFECTION AT FIRST TRIMESTER OF GESTACION: A CASE REPORT

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Problem statement: The coronavirus disease 2019 (COVID-19) can lead to an impairment of liver function tests. Cases of transaminases elevation during pregnancy affected by COVID-19 are rare. ***Methods:*** We report a case of acute non-icteric hepatitis in a pregnant patient at first trimester presenting with COVID-19 infection. ***Results:*** A 41-year-old gravida 4 para 3 at 7 weeks and 5 days of gestation presented to the emergency triage complaining of abdominal pain the right upper. No other symptoms were present such as cough, chills, body ache, vaginal bleeding, at the time of admission. She did a sleeve gastrectomy to 3 years ago. She denied any outpatient medication. Outpatient liver chemistries at her last pre-natal appointment were normal. On admission, her vital signs were stable. Lung examination was normal. Right upper quadrant tenderness and there was no jaundice, hepatomegaly or splenomegaly. Fetal exam was normal. Laboratory values were as follows: serum total bilirubin 1.63 mg/dL, direct bilirubin 0.8 mg/dL, indirect bilirubin 0.83 mg/dL, AST 579 U/L, ALT 353 U/L, GGT 59 U/L, alkaline phosphatase 61 U/L, serum albumin 3.9 g/dL, INR 1.1, lactate dehydrogenase 521 U/L, amylase 65 U/L, lipase 62 U/L, PCR 1 mg/L. Serological tests for acute hepatitis A, B and C were negative. Infectious workup was also negative, except a PCR of COVID-19 that was solicited, which turned out to be positive. Abdominal sonogram revealed a normal liver. After 12 hours, the lab tests were repeated: AST 1075 U/L and ALT 827 U/L. She was monitored in the hospital for 3 days and discharged to home with AST 141 U/L and ALT 461 U/L. At her third month outpatient follow up, AST 11 U/L and ALT 7 U/L. Her pregnancy has since been uncomplicated. ***Conclusion:*** After an exhaustive study to determine the etiology of the elevated transaminases, the hepatic alterations were attributed to SARS-COV2 infection. This pregnant of first trimester presented with acute hepatitis secondary to COVID-19 infection which improved without intervention. The patient progresses with a stable steady decline in hepatic enzyme levels, and at third-month post hospital discharge, her transaminases had reached normal values.

ANEMIA IN PREGNANCY – THE IMPORTANCE OF A GLOBAL ASSESSMENT

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Problem statement: It is estimated that more than 40% of pregnant women have anemia, the two most frequent causes being physiological anemia by dilution and iron deficiency. However, there are other causes that should be considered, such as anemia due to inflammatory/chronic disease or bleeding. ***Methods/Results:*** We present the case of a 32-year-old pregnant woman with a history of epilepsy, asthma and hyperthyroidism. She went to the emergency room at 7 weeks of gestation with epigastric pain. Analytically she had a hemoglobin of 8. At this time, as the patient did not present blood loss or anomalies on the gynecological exam, she was discharged medicated with oral iron and scheduled for an appointment for Obstetrics, Immunohemotherapy and Gastroenterology. At 9 weeks + 3 days of pregnancy, she returned to the emergency room with asthenia, dizziness, dark stools and hematochezia. On gynecological examination there were no significant changes, but on rectal examination she presented black stools with reaction to hydrogen peroxide. Analytically, hemoglobin of 5.2 and elevated hepatic transaminases, alkaline phosphatase, gamma-glutamyl transpeptidase and lactate dehydrogenase were

highlighted. At this point, it was decided to hospitalize the patient for blood transfusion, maternal surveillance and stabilization, and investigation of the condition. The patient received 10 units of erythrocyte concentrate during 10 days of hospitalization. After an abdominopelvic ultrasound, upper digestive endoscopy, colonoscopy with biopsies and magnetic resonance imaging, she was diagnosed with an ulcerated bleeding colon adenocarcinoma with diffuse liver metastization. The patient chose to medically terminate the pregnancy, which was uneventful, and started chemotherapy after evaluation in an Oncology appointment. ***Conclusion:*** This case highlights the importance of evaluating the pregnant women`s anemia as an all. We should not assume physiological anemia or iron deficiency in all cases. In bleeding cases we should search for the source, after exclude obstetric/gynecological complication. Furthermore, it should be considered that, despite remaining rare, the incidence of cancer in pregnant women has increased, which is why it is also an important diagnosis to consider.

HETEROTOPIC PREGNANCY – A CLINICAL CASE

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Problem statement: A heterotopic pregnancy occurs when there are two simultaneous pregnancies with different implantation sites, the majority being an intrauterine pregnancy and a tubal pregnancy. Heterotopic pregnancy is a rare entity with an incidence of 1 in every 30,000 pregnancies. However, this number has been increasing due to medically assisted reproduction techniques. ***Methods / Results:*** We present a case of a 31-year-old woman, with a spontaneous pregnancy, who went to the emergency department due to mild vaginal bleeding without associated pain. During physical examination there was no vaginal bleeding and an ultrasound showed a gestational sac in utero compatible with approximately 5 weeks. She was discharged with an indication to maintain surveillance. About 3 weeks later, she returned to the emergency department due to severe abdominal pain, vomiting and general malaise. Physical examination revealed marked skin and mucosal pallor, blood pressure of 55/33 mmHg, absent vaginal bleeding and palpation of the right iliac fossa with pain. The ultrasound showed a gestational sac in utero with an embryo with cardiac movements compatible with 8 weeks and a retrouterine heterogeneous mass. At this point, an emergent exploratory laparoscopy was decided, during which a large hemoperitoneum was aspirated and a right salpingectomy was performed after verifying that the right tube was ruptured. The left tube and ovary had no apparent alterations. During hospitalization she received 4 units of erythrocyte concentrate and 2 units of plasma. She was discharged on the fifth postoperative day, stable and maintaining a viable intrauterine pregnancy. Later, pathological anatomy confirmed the ectopic pregnancy in the excised tube and, therefore, a heterotopic pregnancy. ***Conclusion:*** The clinical case shows the importance of remembering this entity and its possible consequences when evaluating an early pregnancy. It is always necessary to carry out a careful evaluation of the adnexa, especially in early pregnancy. It is important to identify this entity early before it causes hemodynamic instability.

LIFE-THREATENING HAEMORRHAGE POST UTERINE ASPIRATION IN A FIRST TRIMESTER PREGNANCY LOSS

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Problem statement: Early pregnancy loss, which occurs in the first trimester (up to 12+6 weeks), is the most common type of miscarriage. Expectant, medical, or surgical management are adequate options when retained products of conception are present. Even when more conservative management is adopted, uterine evacuation could be necessary if retained tissue persists. Acute haemorrhage after first-trimester uterine vacuum aspiration is uncommon and can result from uterine atony, cervical or vaginal lacerations or retained tissue. Abnormal placentation is a rare cause of severe bleeding but can be present in the late first trimester. This situation must be considered if prior caesarean delivery or other uterine surgeries. ***Methods:*** We report a case of acute uterine bleeding with hypovolemic shock after a first trimester uterine evacuation, not reversable with standard therapies measures. ***Results:*** A 37-year-old woman with prior caesarean delivery and two miscarriages, presented with an early pregnancy loss. The ultrasound revealed an intrauterine pregnancy with a gestational sac containing a 5.6mm embryo without heart activity. Due to medical management failure, it was performed a uterine vacuum aspiration with complete remotion of retained tissue under ultrasound control. In the end of this procedure, a heavy uterine bleeding with hemodynamic instability was noted. Fluid resuscitation and blood product replacement was initiated. Implementation of primary treatment measures: uterine massage, rectal misoprostol, oxytocin perfusion failed to revert the haemorrhage. The next step was intrauterine tamponade with a 30cc standard Foley catheter with bleeding control and progressive clinical stabilization. The patient was transferred to intensive care unit. Postoperatively remains hemodynamically stable, with catheter removal 42 hours later and clinical discharge at day 5. ***Conclusion:*** Uterine tamponade can be an effective intervention for controlling haemorrhage refractory to massage and uterotonics and should be considered early in this process. The uterine oxytocin receptor concentration is low in first trimester and therefore oxytocin perfusion is contradictory. A Foley catheter is a very disponible device that can be used in this situation. Abnormal placentation or a small arterial laceration could be the reason of this massive haemorrhage in our patient. The uterine tamponade avoided uterine embolization or hysterectomy.

FACTORS RELATED TO MATERNAL MORTALITY WITH COVID-19 INFECTION

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Problem statement: The number of maternal deaths with COVID-19 infection in Indonesia increase significantly in 2021 and will get worsen as the second wave continues. The Indonesian Obstetrics and Gynecology Association (POGI) stated that until April 2021, 536 pregnant women in Indonesia were exposed to COVID-19, and of that number, 16 died. Understanding the evidence of maternal mortality with COVID-19 infection and their worsening factors is essential in providing the best possible health care. ***Method:*** This is a retrospective study of 155 pregnant women infected with SARS-CoV-2 at Dr. Sardjito Hospital Yogyakarta from January 2020 to June 2021. The subjects were grouped into 55 nonsurvivors and 100 survivors and the medical record data for laboratory and radiological findings were collected. ***Result:*** We found that the levels of Dimerized plasmin fragment D (D-dimer), C-reactive protein (CRP) and lactate dehydrogenase (LDH) were significantly higher in non-survivals on admission: D-Dimer 500 mg/L (449 [188–30.000]; p 0.01), CRP 5 mg/L (62 [3–200]; p 0.01), LDH 190 U/L (391 [188–3185]; p 0.01) while

interleukin-6 (IL-6) did not show a significant different levels. In addition, the radiologic parameter had the greatest value, which means that the radiologic parameter is very influential on the patient`s status. Furthermore, patients with pneumonia conditions are 28 times more likely to die than patients with normal radiologic findings. Then followed by other parameters: IL-6, LDH, and CRP, respectively. While the D-dimer parameter did not show a significant effect on the progression of pregnant patients with COVID-19 infection to a mortal condition.Conclusion: There are no specific therapeutic agents for coronavirus infections are available; therefore, the early identification and in-time treatment of severe cases are very important for managing these patients.

Keywords: *maternal mortality, COVID-19 infection*
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Conflict of Interest: *There are no conflicts of interest.*

ASSOCIATION OF NEUTROPHIL TO LYMPHOCYTE AND PLATELET TO LYMPHOCYTE RATIOS TO GESTATIONAL DIABETES MELLITUS: PREDICTIVE VALUE FOR EARLY DIAGNOSIS DURING FIRST TRIMESTER PREGNANCY AMONG PATIENTS SEEN AT A TERTIARY HOSPITAL. A PROSPECTIVE STUDY

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Background: GDM has both detrimental maternal and fetal effects. Early screening, diagnosis and management is crucial. Availability and affordability of glucose tests pose a problem in rural, far-flung and poor areas. The ease of doing and compliance of patients with glucose tests warrant a simpler and cheaper option. Complete blood count (CBC), specifically neutrophil to lymphocyte and lymphocyte to platelet ratios (NLR, PLR) have been shown to be correlated with GDM. ***Objective:*** This study aimed to establish a correlation and strengthen the utilization of inflammatory and hematologic ratios in predicting GDM during the first trimester among Filipinos. ***Methods:*** A prospective cohort approach with 300 patients enrolled in the study. Initial CBC and 75g OGTT results were gathered during the 1st trimester. Subsequent 75g OGTT during their 24-28th week age of gestation were documented and classified according to IADPSG guidelines. ***Discussion and Conclusions:*** A strong correlation was found between NLR and PLR, and the early detection of GDM. The optimal cut off points based on ROC Curve Analysis are 3.29-3.42 for NLR and 985.19-1016 for PLR. The sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were as follows: 0.38, 0.848, 0, 0.588, 0.542, 1.425 and 0.845 for NLR and 0.82, 0.24, 0.519, 0.571, 1.079 and 0.75 for PLR. Findings of the study suggest that both NLR and PLR can be important markers for GDM screening in the 1st trimester.

ADVANCED MATERNAL AGE AND OBSTETRIC OUTCOMES ACCORDING TO PARITY

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Problem statement: The identification of high-risk pregnancies is critical. Advanced maternal age has been systematically considered a risk factor and it´s impact seems to be influenced by parity. This study aims to compare obstetric outcomes above vs. below 40 years of age in nulliparous and multiparous women. ***Methods:*** Retrospective consult of the records of all patients with delivery after 24 weeks gestation in Hospital do Espírito Santo de Évora (Portugal) in 2017 and 2018 (previously to the COVID-19 pandemic). Our sample included 2216 women: 1083 nulliparous and 1133 multiparous (51,1%). The minimum age was 14 years, the maximum 47, and the average 31 (≤17 years: 30 patients; 18-29 years: 800; 30-39 years: 1228; ≥40 years: 158). The data was analyzed with SPSS. ***Results:*** Advanced maternal age was associated with:

-Deliveries by cesarean section -in nulliparous and multiparous women (nulliparous: ≥40 years: 53,5%; 40 years: 32,1% -χ2 p=0,003; multiparous: ≥40 years: 47,8%; 40 years: 32,3% -χ2 p=0,001)

-Non-urgent cesarean sections -in nulliparous women (≥40 years: 62,5%; 40 years: 30,8% -χ2 p=0,006)

-Cesarean sections as a result of fetal distress or a pathological condition related to pregnancy -in multiparous women (≥40 years: 38,9%; 40 years: 24,9% -χ2 p=0,026)

-Preterm births -in multiparous women (≥40 years: 18,6%; 40 years: 7,5% -χ2 p0,001)

-Twin deliveries -in multiparous women (≥40 years: 3,5%; 40 years: 1,1% -χ2 p=0,05)

There were no differences in induction of labor, birthweight, Apgar Score, fetal or maternal mortality.

Conclusion: The data from our Center does support that advanced maternal age is associated to worse obstetric outcomes and that such association is influenced by parity. Most notably, cesarian sections were increased in women with deliveries at 40 years of age or above. In the nulliparous subgroup these numbers seem to have been driven by a lower threshold for intervention in older woman. However in the multiparous subgroup the driving force appears to have been a higher incidence of fetal distress and pathological conditions related to pregnancy (like pre-eclampsia or intrauterine growth restriction); there were also more preterm births and twin deliveries.

FETAL MACROSOMIA AND OBSTETRIC OUTCOMES: UNREAL REAL-WORLD DATA

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Problem statement: Cesarian sections have short and long-term consequences and risks. A limited number of clinical scenarios justify such intervention. An estimated fetal weight ≥4000g is considered to be one of them. Is important to know if real-world data supports this option. This study compares the obstetric outcomes of neonates with normal and macrosomic birth weights. ***Methods:*** Retrospective consult of the records of all patients with delivery in Hospital do Espírito Santo de Évora (Portugal) in 2017-2018 (previously to COVID-19) (n=2216). Selection of neonates with a birth weight of 2500-3999g or ≥4000g. The final sample included 1967 cases (normal weight: 1896; macrosomic: 71). The data was analyzed with SPSS. ***Results:*** **The 2 groups had NO significant differences in:**

-**Apgar Score 7 at 5min** (normal weight: 0,3% vs. macrosomic: 0,0%)

-**Type of delivery** (normal weight: 53,4% unassisted vaginal delivery; 17% assisted vaginal delivery; 29,5% cesarian section vs. macrosomic: 50,7% unassisted vaginal delivery; 14,1% assisted vaginal delivery; 35,2% cesarian section)

-**Cesarean sections as a result of fetal distress** (normal weight: 23,8% vs. macrosomic: 8,3%)

-**Urgent cesarean sections** (normal weight: 44,7% vs. macrosomic: 48%)

There were only significant differences in:

-**Induction of labor** (normal weight: 25,5% vs. macrosomic: 40,0% -χ2 p=0,006)

Conclusion: Our Center is the only Obstetric Department within a large radius and serves a diverse population. The majority brings a third trimester ultrasound but its quality varies greatly. In this setting neonates with normal and

macrosomic birth weights had similar obstetric outcomes. It is possible that our reference should be ≥4500g.

INCREASING PREVALENCE OF LABOUR INDUCTION; HAS IT HAD ANY IMPACT ON THE PREVALENCE OF ADVERSE PREGNANCY OUTCOMES? A POPULATION STUDY IN NORWAY 1999-2019

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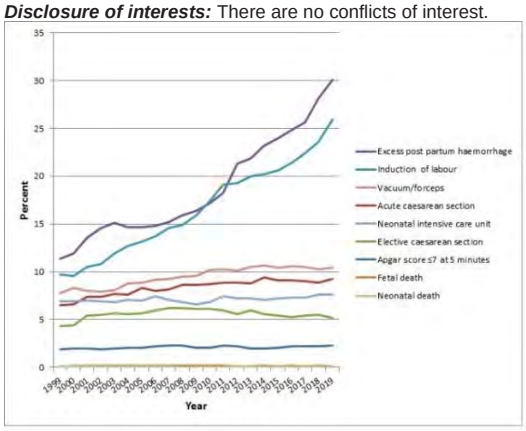
Problem statement: Induction of labour in term and particularly in post term pregnancies has been increasingly common. The rationale for induction of labour is to prevent adverse pregnancy outcomes. We wanted to study whether changes in the prevalence of labour induction are accompanied by changes in adverse pregnancy outcomes or mode of delivery. ***Methods:*** We performed a population-based register study with data from the Medical Birth Registry of Norway. We included all singleton births at gestational weeks 37-42 in Norway, 1999-2019 (n=1 127 945). Our main outcome measures were: adverse perinatal outcomes (Apgar score ≤7 at five minutes, admission to the neonatal intensive care unit, fetal and neonatal death), mode of delivery (acute and elective caesarean section, vacuum and/or forceps assisted delivery) and post partum haemorrhage 500 millilitre. We calculated the prevalence (percent of total) of labour induction and outcome measures according to year of birth. We repeated these calculations for each gestational week at birth. ***Results:*** During 1999-2019, the prevalence of labour induction increased from 9.7% to 25.9%. The increase was high independent of gestational week at birth. The overall decline in fetal deaths was small. Particularly had the decline in gestational week 42 little impact on the overall prevalence. There were no overall changes in the prevalence of newborn with Apgar score ≤ 7 at birth, admission to the neonatal intensive care unit or neonatal death. The proportion of women with excess post partum haemorrhage increased from 11.4% to 30.1%. The increase was independent of gestational age at birth, and was observed both in pregnancies with and without labour induction, even though the prevalence was higher when labour was induced. The prevalence of operative deliveries increased slightly. ***Conclusions:*** Despite a large increase in induction of labour, we found only a small decrease in fetal deaths and no decrease in other adverse perinatal outcomes. The prevalence of excess postpartum haemorrhage increased dramatically.
Disclosure of interests: There are no conflicts of interest.



DETECTION OF CHROMOSOMAL ABNORMALITIES IN SPONTANEUS MISCARRIAGE IN THE FIRST TRIMESTER BY CGH AND NEXT GENERATION SEQUENCING

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Spontaneus miscarriage (SM) is a major cause of pregnancy failure. It is estimated that10-15% of all clinically recognized pregnancies terminate in SM. In addition 50% af all SMs have chromosomal abnormalities (CAs)
Introduction: Conventional methods used to detect CAs and determine the cause of pregnancy loss include karyotyping, fluorescence in situ hybridization, quantitative fluorescent-PCR (QF-PCR) and multiplex ligation-dependent probe amplification. However, these methods have inherent limitations. Following the rapid development of molecular biology technologies comparative genomic hybridation (CGH) have become the standard methods used to investigate possible chromosomal cause but high cost, low throughput and requirement of high-quality DNA are the limitations. Recently the NGS is applied without the drawbacks. In this study we present the results, using QF-PCR / Array-CGH and NGS in abortive remains of the first trimester, trying to establish a relationship with the method of pregnancy, age, and the number of previous abortions.
Materials and methods: From 2015 to July 2021, 188 abortions were studied, 121 QF-PCR / Array CGH and 67 NGS. 24 are excluded by maternal contamination.31 are from ART (without PGT-A or egg donation), whit average age 37,9 and 133 SM whit 37,3. ***Results:*** In the table we can see the results comparing TRA whitout TRA.12,7% was maternal contamination. Patients without TRA the distribution by age was 50% for ≥ 29 years, 66% for 30-34 years and 70% ≥ 35.In 109 cases whit previous abortions we didn´t found more Cas. ***Conclusions:*** The CGH and NGS techniques have allowed us to diagnose 64% of CAs. In TRA patients the alteration rate is less than spontaneus pregnancy. Other endocrine, uterine and inmunological factors can interfere whit results.The most commun CAs are autosomal trisomies (66%), the most common being T16,T22,T15, and T22. In SM T16,T22 and T15 are associated whit high probabilities of fetal death, anomalies, preterm delivery and intrauterine growth retardation. The X monosomy and its variants are 13%, and triploidies 12%.In conclusion CAs are the most common causes of abortion in SM whit trisomy being the most frequent.

STUDY OF CLINICAL DIAGNOSTIC AND LABORATORY CRITERIA FOR THE PREDICTION OF PREECLAMPSIA IN THE FIRST TRIMESTR OF PREGNANCY

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Preeclampsia is one of the leading causes of maternal mortality. It is found after the 20th week of pregnancy and is characterized by hypertension, proteinuria, gestational edema, and eclampsia, could leading to maternal death. The purpose of this article was to study the risk factors for preeclampsia, as well as to predict preeclampsia using diagnostic (Doppler) and laboratory markers (B-2 glycoprotein-1, XQ, PAPP-A, placental height factor) until. According to the results of the study, the presence of chronic hypertension in previous pregnancies (PV + 100%), history of preeclampsia and eclampsia (PV + 83.3%), vaginal bleeding in current pregnancies (PV + 83.3%), a combination of 3 and more risk factors (PV + 85.2%) was assessed as a high risk factor for preeclampsia. Preclinical

laboratory markers of preeclampsia include elevated B-2 glycoprotein-1 and human chorionic gonadotropin, decreased placental growth factor, and decreased PAPP-A levels in the blood. The most important factors in the prognosis of hypertensive disorders were placental growth factor (PV + 93.8%) and B-2 glycoprotein-1 (PV + 88.9%). Early dopplerometric indications for preeclampsia include dichroic carving and decreased uterine-double blood flow. Dopplerometric indicators of severe preeclampsia - RI up to 0.60 and dichrotic notch in both uterine arteries or RI between 0.61-0.70 and only one uterine artery with dichrotic notch and no dichrotic notch in the uterine arteries Above 0.70 - can be used as prognostic markers. *There is not any disclosure of interest.*

PREVALENCE OF INFLAMMATORY AND VASCULAR PLACENTAL LESIONS IN COVID-19 POSITIVE PREGNANT WOMEN

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Problem statement: Coronavirus disease 2019 (COVID-19) infection can cause a systemic inflammatory response which has been related with a hypercoagulable state, and with the presence of microangiopathic disease and venous thromboembolism in most organ systems. Furthermore, the virus can be transmitted to the fetus with high viral loads through the placenta, increasing the possibility that it may cause placental injury. Our study aimed to evaluate alterations in the microvascularization of the placentas and the umbilical cords that may translate into a predisposition to thrombosis in COVID-19 positive patients during pregnancy. ***Methods:*** Pregnant women infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who attended to Vall d'Hebrón Hospital (Spain) were included. Medical history data from 100 women were evaluated and a histopathological examination of 99 placentas was performed. We evaluated the incidence rates of maternal vascular malperfusion (MVM), fetal vascular malperfusion (FVM) and acute and chronic inflammatory responses present in the placentas. ***Results:*** We observed a very high rate of placentas that presented lesions of vascular and/or inflammatory origin (93% of the placentas). It is noteworthy that 75% of the placentas had multiple vascular or inflammatory lesions. Our results show a high incidence of characteristics of MVM (78%), FVM (58%), and chronic inflammatory response (50%), while the rate of acute inflammatory response was not high (22%). We identified a high prevalence of infarcts (38%) and distal villous hypoplasia (syncytial knots were increased in 37%) among other characteristics of MVM; and a high proportion of placentas presented thrombi in large fetal vessels (20%) and hyalinized avascular villi (38%). A relevant increase in the intervillous fibrin deposits was also observed. ***Conclusion:*** COVID-19 infected pregnant women presented high rates of MVM, FVM and chronic inflammatory response histological characteristics. These alterations reflect anomalies on oxygenation and in blood flow dynamics and relate with adverse pregnancy and neonatal outcomes. Our findings describe the proinflammatory and hypercoagulable state repercussions of COVID-19 in the fetal-maternal unit.

ASSOCIATED INDICATORS WITH NO TREATMENT, INADEQUATE TREATMENT AND DELAYED TREATMENT IN MATERNAL SYPHILIS: A CROSS-SECTIONAL STUDY IN EASTERN CHINA

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Problem statement: To improve adequate and early treatment for maternal syphilis are still challenges. ***Methods:*** A cross-section study was conducted. Data were from the China's Information Management System of Prevention of Mother-to-Child Transmission (PMTCT) of Syphilis in Zhejiang. Maternal syphilis reported during 2014-2020 were included. The demographic characteristics, history of pregnancy and labor, syphilis infection and treatment were assessed. Multivariate logistic regression was used to explore the associated factors with therapy at individual-, county- and hospital level. ***Results:*** A total of 15,473 syphilis pregnant women from 11 cities, 92 counties, and 882 hospitals during 2014-2020 in Zhejiang were enrolled. The overall coverage of treatment, adequate treatment, and early treatment were 92.50%, 72.56%, and 40.50%, respectively. At individual level, to postpone per one week of first antenatal health care (ANC) visit (Odds ratios[ORs]: 1.032 [95%CI 1.024, 1.040], 1.078 [1.072, 1.084], and 1.201 [1.189, 1.212]), to be known partner's syphilis infection status or unscreened (1.591[1.294, 1.957], 1.299[1.171, 1.441], and 1.309[1.202, 1.426]), to identify maternal syphilis at labor(16.341[13.283, 20.103], 25.883[20.509, 32.665], and 5.057[3.913, 6.536]) or after labor(28.346[20.829, 38.576], 26.986[17.016, 42.796], and 6.037[3.505, 10.398]) were strongly associated with no treatment, inadequate treatment, and delayed treatment, respectively. Compared to those who had more than one child, those with only one child were less likely to being treated, inadequately treated, and lately treated, with ORs as 0.697(0.559, 0.869), 0.631(0.548, 0.726), and 0.777(0.674, 0.895), respectively. Maternal syphilis titer beyond 1:8 promoted adequate treatment than the remainders (0.812 [0.718, 0.919]). Maternal syphilis therapy rates also differed significantly across counties and hospitals, presenting MORs as 2.034 at county level and 1.792 at hospital level for treatment, 1.680 vs 1.320 for inadequate treatment, 1.244 vs 1.332 for late treatment. Moreover, GDP per capita (1.068[1.001, 1.139]) was poorly with maternal syphilis therapy. ***Conclusion:*** Despite high coverage of maternal syphilis treatment, adequate and early treatment rates were still poor and varied at individual-, county- and hospital level. The associated factors were multiple. Women with unstable marriage, with late first ANC, without syphilis information for their partner, with syphilis stage as one or above are vulnerable population for treatment.

PRIMARY HYPERPARATHYROIDISM IN PREGNANCY REFRACTORY TO MEDICAL MANAGEMENT: A CASE REPORT

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The incidence of primary hyperparathyroidism (PHPT) in pregnancy is rare but associated with serious maternal and fetal consequences. The principal cause of PHPT in pregnancy is parathyroid adenoma. Clinical manifestations are present in approximately 70% of the diagnosed patients. Treatment is based upon severity, symptoms and gestational age. Surgical approach is preferred for symptomatic hypercalcemic PHPT. We report the case of a

primigravida presenting symptomatic hypercalcemia caused by underlying hyperparathyroidism and that remained symptomatic after aggressive conservative management. Research performed in PubMed databases including the terms “hyperparathyroidism” and “pregnancy”. Case reports and review articles of Primary hyperparathyroidism in pregnancy were selected and the patient’s case was revised. A 22-year-old woman with a medical history of second-degree atrioventricular block was referred to the Department of Endocrinology after a cervical ultrasound prescribed for symptoms of dysphagia. This exam showed a hypoechoic nodule (19 mm x 11 mm x 22 mm) in her left thyroid lobe compatible with parathyroid adenoma. A technetium-99m sestamibi scan confirmed the localization of parathyroid disease. The blood tests revealed elevated S-Ca and parathyroid hormone (PTH) levels. Given her young age, genetic testing to excluded Multiple Endocrine Neoplasia Type 1 and 2 was performed. She become pregnant while on the study of PHPT. At first prenatal appointment a biochemistry evaluation revealed severe hypercalcemia and a hospitalization was proposed. Oral hydration with saline infusions administered intravenously associated to a single dose of cinacalcet were started. However, she developed clinical manifestations of hyperemesis and nausea, her S-Ca level increased and a short QT interval was detected in her electrocardiogram. Surgical removal of her left lower parathyroid gland was done and her level of intraoperative PTH level was 107 pg/ml. Her S-Ca levels were 1.45 mmol/L on the first postoperative day. In order to prevent hungry bone syndrome, vitamin D was started. Nine days after the parathyroidectomy she was discharged from the hospital. The pregnancy follow up is going without significant complications. This case highlights the beneficial role of timely surgical management for severe or symptomatic PHPT in pregnancy and the need for a multi-disciplinary approach for the maternal and fetal wellness.

PRIMARY HYPERPARATHYROIDISM DIAGNOSIS IN PREGNANCY

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Problem statement: Primary hyperparathyroidism (PHTP) is a rare diagnosis in pregnancy with a prevalence rate of 0.05%. The most frequent aetiology is a solitary parathyroid adenoma. Pregnant women are mostly asymptomatic but some develop lethargy, weakness, nausea, vomiting and polyuria which are also frequent early pregnancy symptoms. Diagnosis is made in the presence of hypercalcemia with a non-supressed parathyroid hormone (PTH) level. PTHP can be associated with maternal complications - hyperemesis gravidarum, nephrolithiasis, pancreatitis – and neonatal hypocalcaemia. Management is dependent on the severity of symptoms, gestational age and complications. Mild cases can be managed conservatively whereas in severe cases surgery is the only curative option. ***Methods:*** Case report and literature review. ***Results:*** A 43 year-old-nullipara, with medical history of gastric bypass (due to previous grade lll obesity) and nephrolithiasis was referred to our centre at 11 weeks gestation, for pregnancy surveillance. In early pregnancy she complained of weakness, nausea and vomiting. Her first trimester screening and ultrasound were normal and demand for Endocrinologist follow up was requested due to her medical antecedents. Analytic evaluation with ionic panel performed at 24 weeks revealed anemia - 11.2 g/dL haemoglobin, vitamin B12 and vitamin D deficiency - 185 pg/mL and 18.2 ng/mL respectively, hypophosphatemia - 2.1 mg/dL, hypercalcemia - 11 mg/dL and elevated PTH levels - 177 pg/mL. Thyroid function was normal. Upon these laboratory findings, primary hyperparathyroidism was diagnosed and cervical echography revealed its origin: a parathyroid adenoma. Aspirative cytology was performed, demonstrating high PTH levels - 292 ng/L - in the collected liquid, confirming hyperparathyroidism diagnosis. The patient is currently in the 3rd trimester, remains asymptomatic and with mild hypercalcemia, therefore a conservative management has been adopted so far. ***Conclusion:*** PHTP is a rare diagnosis in pregnant women. Most cases are asymptomatic or develop symptoms similar to those that occur early in pregnancy. High clinical suspicion is paramount for the diagnosis in pregnancy, enabling optimal management with a multidisciplinary approach to provide the best maternal and neonatal care.

THIRD-TRIMESTER PLEURAL EFFUSION – DIAGNOSIS AND APPROACH BASED ON A NOONAN SYNDROME CASE REPORT

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Problem statement: Noonan Syndrome (NS) has a clinical and genetical heterogeneous presentation. It is nearly always an autosomal-dominant disease (50% having a pathogenic variant of the PTPN11 gene) with 1/3 of cases being inherited, not uncommonly by parents unknown of their diagnosis. Should be suspected in cases of increased nuchal translucency (NT), ascites or polyhydramnios and imagiological signs may include kidney and heart anomalies. Prognosis is variable, from antenatal demise to mildly affected adults with normal lifespan. ***Methods:*** To report a case of prenatal diagnosis of NS, using clinical data and reviewing bibliography. ***Results:*** Twenty-five years-old primigravida, unremarkable past medical history. On 1st trimester ultrasound (US), NT above the 99th percentil was diagnosed. Chorionic villus sampling was performed. Qf-PCR and cGH-array were normal. Following US evaluations were normal, namely 2nd trimester nuchal fold. At 25weeks, an echogenic cavum septi pellucidi was observed, which prompted a fetal MRI that identified a slight thickening of the fornix, which persisted when re-evaluated by MRI at 33weeks, of unknown significance. At 32weeks and 6days, moderate volume right pleural effusion was identified, and a next generation-sequencing (NGS) panel for NS most frequente mutations was performed.US scanning were performed on a weekly basis, until 34weeks and 3 days, when moderate polyhydramnios was noted. Fetal lung maturation was iniciated. The following day, bilateral hydrothorax with left shift of mediastinic structures were present. Due to daily progressive worsening of clinical findings, bilateral thoracocentesis and amniodrainage were performed at 35weeks, with almost complete thoracic decompression. Meanwhile, NGS panel revealed the dianosis of NS. Three days later the thoracic fluid had rebuilt and termination of the pregnancy through c-section was decided. Thoracocentisis was repeated just before fetal extraction. Newborn had 2500g and Apgar Index of 7/8/8 and was admitted in the Neonatology Care Unit. A bilateral thoracic drain since 1st day of life was needed as well as octreotide support. ***Conclusion:*** NS accounts for less than 5% of hydrothorax cases, but it’s a diagnose to be kept in mind since it will be missed on Qf-PCR and cGH-array. A genetic cause for fetal hydrothorax may influence surveillance, treatment and prognosis.

EMERGENCY PERIPARTUM HYSTERECTOMIES: A 20-YEAR REVIEW

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Problem statement: Nowadays, emergency peripartum hysterectomy (EPH) is only performed as a life-saving surgery in serious postpartum hemorrhagic situations, when more conservative measures such as medical treatment or less invasive surgical procedures fail. With this retrospective study we aim to evaluate its incidence, indications, risk factors and maternal morbimortality. ***Methods:*** A retrospective analysis of all the EPH performed over the last 20 years in a tertiary care facility was made. ***Results:*** There were 27 cases of EPH among 35439 deliveries, between 2001 and 2021, with an incidence of 0,76:1000 births. 71% were performed during the first 10 years. Over the last 10 years the incidence decrease from 1,17:1000 to 0,38:1000 births. From all the EPH, only 7% were subtotal. The most common indication for this procedure was uterine atony (59%), followed by placental invasion (30%). Uterine inversion or rupture and cervix lacerations were identified as less common causes. Risk factor analysis showed multiparity (75%), cesarean delivery in the current pregnancy (59%), older age (54%) and previous cesarean section (26%) as important contributing aspects for this outcome. There was no mortality registered, however severe morbidity was seen, with hypovolemic shock and intravascular disseminated coagulation as the main complications. ***Conclusion:*** EPH is the most demanding obstetric surgery performed in very exasperating situations of life threatening postpartum hemorrhage. The incidence has been decreasing over the last two decades, probably due to better postpartum hemorrhage care with earlier, faster and improved diagnose and treatment. Simulation training may have an important role in this new reality. Cesarean deliveries prior to or in the current pregnancy are important risk factors since they contribute to abnormal placentation disorders and a higher risk of uterine atony and rupture.

FETAL BOWEL DILATATION ON LATE PREGNANCY: CASE REPORT

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Problem statement: The presence of dilated bowel loops antenatally suggests fetal bowel obstruction. Depending on the level and extent of obstruction, timing of presentation, diagnosis and prognosis may modify. Finding its etiology prenatally is difficult, however differential diagnosis as bowel atresia or stenosis, malrotation with volvulus, meconium ileus, total colonic aganglionosis, and meconium plug syndrome most be thought. Jejunoileal atresia(JIA) is seen in 1:5000-14000live births. It has an important impact in neonates' life so its early diagnosis is key for an optimal treatment and prognosis. ***Report:*** We present a case of a bowel dilatation prenatally diagnosed in a twin girl with 36 weeks. A healthy 40-years woman with a dichorionic-diamniotic gestation presented at 33 weeks to the hospital with high blood pressure. Until that day, there were no pregnancy intercurrences, both babies were on the 35-40thcentile and no abnormalities were described on the ultrasounds. At hospital admission a diagnosis of preeclampsia with no severity criteria was made and some bowel prominence without dilatation criteria was detected on the first fetus. Hospitalization for pulmonary fetal maturation and fetal-maternal surveillance was recommended and accepted by the pregnant. During 3weeks no complications were identified. Nevertheless, at 36 weeks massive bowel dilatation on the first fetus was identified. No other alterations were found. After multidisciplinary discussion, two girls were born at 36weeks and 4days by elective cesarean section, with 2135g and 2030g,respectively. An exploratory laparotomy was performed at first day of life after suspicion of ileal atresia on the abdominal x-ray. Intra-operative findings revealed a single lesion with two separated segments of ileum with a V-shaped gap within the mesentery, confirming a type IIIa ileal atresia. Due to significant size discrepancy between proximal and distal bowel, a temporary ileostomy was performed. Enteral feeding was introduced in the 4th post-operative day. ***Conclusion:*** JIA is a common cause of intestinal obstruction in neonates. Distal intestinal atresia more commonly presents with sonographic findings more lately in pregnancy. Occasionally, it is associated with other malformations such as cardiac anomalies, gastroschisis, and cystic fibrosis. Antenatal detection is crucial to determine is management, including time of delivery with early resuscitation and prompt surgical intervention available.

A CASE STUDY REPORT: DELAYED DIAGNOSIS OF SECOND TRIMESTER ABDOMINAL PREGNANCY

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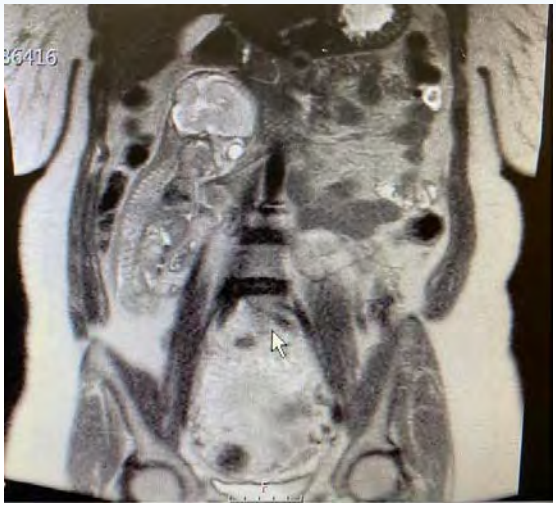
Problem statement: Abdominal Pregnancies are a rare form of ectopic pregnancy that often carry a high risk of maternal morbidity and mortality within the first trimester of pregnancy. ***Methods:*** We describe the unusual case of late diagnosis of an abdominal pregnancy in the second trimester which was not diagnosed on early pregnancy routine obstetric scans, in a 35-year-old Black-African woman. Diagnosis was made at repeat anomaly scan at 21 weeks + 3 days and confirmed with MRI, further management and MDT involvement. Our case's rarity was identified as a case where the baby was originally in the amniotic sac surrounded by normal liquor volume, the placental site was well visualized and attached closely to the fundus of the uterus. The transvaginal and transabdominal scans showed that this was an intrauterine pregnancy coupled with an endometrium mimicking that of the cervix. The uterus was visualized, and the diagnosis of an abdominal pregnancy was made possible after the rupturing of the sac, leading to anhydraminos which caused the baby to move from the pelvic region to the upper maternal abdomen. ***Results:*** The patient underwent a laparotomy, delivery of the baby, excision of the placenta, left salpingo-oophorectomy and omentectomy as an emergency procedure under general anaesthetic. Operation findings indicated an intact uterus, and the placenta was embedded at the left Cornua. The baby was identified extrauterine and delivered in a poor condition. ***Conclusion:*** The diagnosis of abdominal pregnancy requires a high index of suspicion and extensive understanding and interpretation of the clinical and radiological findings. There is currently no widely accepted diagnostic criteria for abdominal pregnancies and the current criteria available is only for primary abdominal pregnancies, which is based on Studdiford standards. Standardization of the treatment principles for advanced abdominal pregnancy, perioperative treatment and postoperative management measures would improve newborn survival, reduce complications and mortality.
Disclosure of interest: *no interests to disclose.*



PREGNANCY COMPLICATED BY SEIZURES: A PERINATAL EMERGENCY CASE REPORT

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Problem statement: Seizures during pregnancy complicate 1% of all gestations. They are associated with adverse maternal and perinatal outcomes. The differential diagnosis of seizures in pregnancy is extensive. Determining its etiology is crucial to the proper management of these patients. Seizures in pregnancy can be classified into three categories: 1) can occur independently from the pregnant state, 2) are exacerbated by the pregnant state, 3) are unique to the pregnant state. ***Methods:*** The aim of this case report is to increase awareness and discuss an appropriate approach for the diagnosis of pregnancies complicated by seizures. ***Results:*** A 38-year-old primigravida with history of diabetes mellitus type 1 and chronic hypertension, identified with autoantibodies against alpha-methyldopa at 16 weeks of pregnancy and medicated with insulin and nifedipine, came to a routine appointment at 33 weeks and 6 days' and complained of elevated blood pressure (BP145/95mmHg), epigastric pain, edema and fasting hypoglycemias of 30-40mg/dl in the last week. The patient was admitted at the emergency department for evaluation, where she began having tonic-clonic seizures with loss of consciousness. The BP at the time of admission was 182/102mmHg and the pre-eclampsia routines were all negative, including a 24-hour urine proteinuria. An emergent caesarean section was performed (female newborn, 2835g, APGAR score 3/8/10), complicated with uterine inversion and maternal asystole needing cardiopulmonary resuscitation. She was admitted to Intensive Care Unit developing the following complications: persistent loculated pleural effusions, deep venous thrombosis of inferior vena cava and pulmonary thromboembolism and encephalopathy of unknown etiology. Currently with a possible diagnosis of systemic lupus erythematosus under study. ***Conclusion:*** Pregnancies complicated by seizures are a life-threatening emergency that needs a prompt approach and management. The distinction of etiology is critical; therapy must be directed at the underlying disorder as well as at seizure control and post-partum approach. In this clinical case, we see an overlap of hypoglycemia with a possible diagnosis of eclampsia, both manifested through seizures. There was a strong suspicion of an atypical manifestation of pre-eclampsia (no proteinuria or other altered blood tests) as well as multiple risk factors that could lead to catastrophic consequences.

WHEN INSUFFICIENT PRENATAL CARE IS LINKED TO PRETERM BIRTH - A CLINICAL CASE

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Problem statement: Timely management of cervical insufficiency ***Methods:*** Checking the clinical information of the patient in our unit`s server. ***Results:*** A 30 year old woman was sent to our unit with threatened preterm birth (PTB) at 27w+2d. The patient had history of gestational diabetes and gestational hypertension. The current pregnancy was conceived through IVF. T0P1A1L0, both pregnancies conceived through IVF, one resulted in a spontaneous abortion, the other in preterm labour of twins (23w), linked to cervical insufficiency (CI). The speculum exam evidenced an opened cervix with a protruding amniotic sac. The ultrasound showed a live fetus, cephalic presentation and a cervical length of 6mm with funneling. The patient was admitted and started bed rest, tocolysis, corticotherapy, magnesium sulphate and antibiotic prophylaxis. Whilst hospitalized the patient maintained a slight Trendelenburg position, periodic sonograms, physiotherapy, regular bloodwork and therapeutic adjustments. At 31w+5d the patient started exhibiting lumbar and abdominal pain. A cesarean section was performed, to which a live female baby with 1620g was born. ***Conclusion:*** PTB is a major cause of neonatal morbidity and mortality. One of the most significant risk factors for PTB is a history of preterm delivery, and one etiology of PTB is CI. The obstetric history of this patient demanded a close evaluation of the cervical length, progesterone use and, according to guidelines, a prophylactic cerclage. Neither of these procedures were performed and additionally, on arrival at our unit, an emergency cerclage was not an option due to the advanced gestational age. Even though the patient gave birth to her first live newborn, a prompt follow-up and management would have been of utmost importance and could have improved the fetus prognosis.

PRETERM PREMATURE RUPTURE OF MEMBRANES: A CHALLENGE IN FETOMATERNAL MEDICINE

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Problem statement: Preterm Premature rupture of membranes (PPROM) is the rupture of the fetal membranes before 37 weeks of pregnancy. It is responsible for one third of preterm births and also accounts for a major risk of infectious complications to the mother and newborn. The approach may consist of watchful waiting with a rigorous evaluation of infection signs. The management of PPROM is one of the most debated issues in fetomaternal medicine since it is difficult to define the proper time for intervention, balancing between fetal development and infection risk. ***Methods:*** We present two cases of PPROM that were admitted at hospital and had an expectant management. In both cases the initial infection screening was negative. They did a single 7 day course of empiric antibiotics. ***Results:*** Patient A, 25 years-old, first pregnancy, no past medical history. PPROM date was 25weeks and 2 days. Labour occurred at 30 weeks, having a total of 34 days of ruptured membranes. A male was born, weighting 1450g with Apgar score 6/7. He required mechanical ventilation. The newborn stayed at neonatal unit during 47days. It was identified ESBL microorganism colonization, without developing clinical signs of infection. Pregnant B, 38 years-old. She had four prior in vitro fertilization (IVF) that were unssucessful and this pregnancy was also a result of IVF. Ultrasound performed at 23 weeks revealed short cervix

and PPROM occured at 24. The labour happened at 29 weeks, with a total of 42 days of ruptured membranes. The newborn was a female, weighting 1475 with Apgar score 6/8. She was not intubated after delivery but then required respiratory support due to respiratory distress syndrome and later developed sepsis, needing a course of broad-spectrum antibiotics. After 35 days she was discharge from hospital. In both cases there were no significant maternal elevation of infection markers during hospital admission and no complications in postpartum period. ***Conclusion:*** Even though PPROM is a major risk for prematurity and infection complications, it is possible to extend pregancy and achieve favourable outcomes with an expectant approach. The management should be individualized.

A NOVEL ARTIFICIAL INTELLIGENCE APPROACH FOR THE AUTOMATIC DIFFERENTIATION OF FETAL OCCIPUT ANTERIOR AND NON-OCCIPUT ANTERIOR POSITIONS DURING LABOR

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Problem statement: The knowledge of the fetal occiput position is of major relevance in the management of protracted labor, as malposition of the fetal head is associated with an increased risk of obstetric intervention, failed operative vaginal delivery, and adverse maternal or perinatal outcomes. In this study we describe a newly developed Machine Learning (ML) algorithm for the automatic classification of fetal occiput position at transperineal ultrasound (TPU) during the second stage of labor. ***Methods:*** Multicenter international prospective study including 15 Maternities and conducted on singleton term pregnancies with cephalic presenting fetus in the second stage of labor. Firstly, transabdominal ultrasound wasperformed to assess the fetal occiput position, which was labelled into occiput anterior (OA) or non-OA and represented the gold standard reference for training and validation. Secondly, sonographic images of the fetal head were acquired with TPU on the axial plane and archived on a cloud for remote analysis. A ML algorithm based on a pattern recognition feed-forward neural network was developed from transperineal images. In the training phase the algorithm was trained on labeled data (training dataset) in order to assess the fetal head position by evaluating the geometric, morphological and intensity-based features of the images. In the testing phase, the diagnostic accuracy of the algorithm was evaluated on unlabeled data (testing dataset). TheCohen's kappa (k) evaluated the agreement between the ML algorithm and the gold standard. ***Results:***1219 cases were enrolled, of whom 70% were randomly assigned to the training dataset (n=824) and the remaining (n=395 patients) to the testing dataset. 801 (65.7%) had OA position. The ML-based algorithm correctly classified the fetal occiput position in 90.6% of cases (357 out of 395), including 224/246 (91.0%) OA and 133/149 (89.3%) non-OA positions. A high agreement between the ML algorithm and the gold standard method was also noted (k= 0.81; p 0.0001). ***Conclusions:*** A ML algorithm for the automatic assessment of the fetal head position at TPU has been developed, and can accurately distinguish OA and non-OA positions starting from ultrasound images acquired on the transperineal axial plane.

PREDICTION OF CEPHALO-PELVIC DISPROPORTION BY EVALUATING THE RATIO BETWEEN THE HEAD CIRCUMFERENCE AND THE OBSTETRIC CONJUGATE

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Problem statement: Cephalo-pelvic disproportion is one of the biggest challenges of modern obstetrics. It is associated with adverse maternal and neonatal outcomes and with a higher risk of operative delivery. The aim of our study is to evaluate the performance of the ratio between the fetal Head Circumference (HC) to the Obstetric Conjugate (OC) (HC/OC ratio) in the prediction of the mode of delivery. ***Methods:*** Prospective cohort study conducted at two tertiary maternity units (Parma University Hospital and St. Joseph Krankenhaus, Berlin). Women with singleton pregnancy and cephalic presenting fetus were enrolled during antenatal visits performed between 34 and 37 weeks of gestation. During their first visit, ultrasound measurement of the OC was obtained, while the HC was measured on hospital admission for spontaneous onset of labor or labor induction. Maternal and neonatal characteristics, OC and HC values were compared among women who had a vaginal delivery with those who delivered by cesarean section (CS) for labor dystocia. The predictive value of the HC/OC ratio was tested by means of ROC curve analysis. ***Results:*** We included 127 women, of whom 11 underwent CS for labor dystocia. Maternal and neonatal characteristic including OC values did not differ between both groups. A significant difference of the HC (344 ± 13.6 mm vs 362 ± 15.4 mm, p 0.001) and the HC/OC ratio (2.91 vs 3.13, p = 0.009) was found between the two groups. At ROC curve analysis the AUC of the HC/OC ratio for the prediction of a CS for labor dystocia was 0.72. ***Conclusions:*** Preliminary results from this study reported that HC/OC ratio seems to be a good sonographic predictor of cephalo-pelvic disproportion. Larger sample size is needed to confirm our findings.

PREECLAMPSIA CASES PATTERN DURING COVID-19 PANDEMIC: A DESCRIPTIVE STUDY

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Problem statement: Preeclampsia complicates pregnancy and was the main cause of maternal and perinatal morbidity and mortality. Women infected by coronavirus disease 2019 (COVID-19) had higher rates of preeclampsia. Despite numerous publications related to the pandemic, we have all faced unprecedented challenges caring for pregnant women during the COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus (SARS-COV-2) because of limited data, experience and rapidly evolving guidelines. This study aimed at providing data based on our experience on treating preeclampsia during COVID-19 pandemic in our center. ***Methods:*** This was a retrospective, descriptive study. We collected 314 samples on any type of preeclampsia developed in patients, with or without COVID-19, from April 2020 to June 2021, in Kandou Hospital Manado. All data was obtained from medical records. ***Results:*** This study revealed 70 patients indicated COVID-19 infection. 293 patients were delivered with Cesarean section. The maternal age group to developed preeclampsia is aged 20-34 (183 patients), 34 (104

patients) and 20 (27 patients). The types of preeclampsia were severe preeclampsia (178 cases, 39 had reactive SARS-COV-2 antibody results which 3 of them lead to fetal distress and 1 oligohydramnios, 7 were confirmed COVID-19, 2 were COVID-19 suspects, 1 had positive SARS-COV-2 antigen results, 3 were delivered vaginally), impending eclampsia (53 cases, 2 had reactive SARS-COV-2 antibody results which one of them lead to fetal distress, 1 were COVID-19 suspect, 1 were probable COVID-19 ended to fetal death), preeclampsia without severe features (38 cases, 14 had reactive SARS-COV-2 antibody results), eclampsia (24 cases, 3 had reactive SARS-COV-2 antibody results), haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome (21 cases), and superimposed preeclampsia (11 cases). 11 patients developed more than one type of preeclampsia. ***Conclusion:*** Severe preeclampsia patients had the most variety of COVID-19 indication of infection and they lead to fetal distress. All patients confirmed with COVID-19 had severe preeclampsia. Impending eclampsia patients and probable COVID-19 lead to fetal death. These particular group of patients should be considered as vulnerable cases with regard to the risks posed by COVID-19, even though further research may be required.

PREVENTING HEMORRHOIDS AND FISSURES OF PREGNANCY: RESULTS OF THE RANDOMIZED CONTROLLED TRIAL

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Problem statement: Perianal disease (PD) is common in pregnancy and post-partum period. Most relevant risk factor for PD is constipation. Dietary and behavioral changes may reduce the relevance of constipation as well as PD. No studies have evaluated the prevention of constipation with the reduction of the risk of PD. ***Methods:*** Pregnant women who consented to participate in the study were randomly assigned during the first trimester of pregnancy to dietary and behaviour intervention, aimed at prevention on constipation, prolonged straining and reduced time on the commode (intervention group - IG) or to routine pre- and perinatal care (control group - CG). Women were followed up until after the childbirth. Gynaecologists, who were discharging the women from the maternity units and who were blinded to the randomization allocation, filled a questionnaire regarding perianal signs and symptoms and presence of perianal disease. Presuming baseline risk of 35% and reduction of risk to 17%, the level of significance α of 5.0%, power (1-β) of 80%, the sample size was calculated to be 206 patients. The sample size was increased by 30% to 260 to account for losses to follow-up and terminations of pregnancies. The study was approved by the Vilnius Regional Bioethics Committee, Vilnius, Lithuania on the 10th of May 2016, registration number 158200-16-843-357. ***Results:*** 260 women were included in the study from 2016 to 2019 in the three centres. The demographic, clinical, obstetric and medical history characteristics were equal between the groups during the first trimester of pregnancy. 218 women completed the study - 102 in the IG and 116 in the CG. 20 women in the IG (20%) and 53 women in CG (47.8%) were diagnosed with postnatal perianal disease, p0.001. There were 2 cases of spontaneous abortions in the IG and 5 cases in CG, P=0.32, ***Conclusion:*** Women, who were assigned to dietary and behaviour recommendations aimed at preventing constipation and prolonged straining were twice less likely to suffer from symptoms of perianal disease after childbirth. There was no increased risk of pregnancy loss in the intervention group so these recommendations are safe enough to be given to pregnant patients.

WHEN TO SUSPECT OF OTHER TYPES OF DIABETES DURING PREGNANCY – A CLINICAL CASE OF MATURITY ONSET DIABETES OF THE YOUNG (MODY)

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Problem statement: Maturity onset diabetes of the young (MODY) is a type of noninsulin-dependent diabetes, usually diagnosed at a young age. It is frequently misdiagnosed as either type 1, type 2 or gestational diabetes. It is caused by a monogenic mutation, with autosomal dominant transmission. Several genetic abnormalities have been identified, with one of the most affected genes being the glucokinase gene (CGK). These anomalies may lead to impaired glucose sensing or decreased insulin secretion. One of the main concerns during pregnancy is knowing when to initiate insulin therapy, as a higher risk of neonates below the 25th percentile has been described in cases where both the mother and the fetus have the mutation and insulin therapy is instituted. ***Methods:*** Retrospective description of a clinical case. ***Results:*** We describe the case of a 35-year-old woman, with autoimmune hypothyroidism and a clinical suspicion of diabetes in her childhood. This hypothesis was raised due to fasting mild hyperglycemias, though she never had a value above the cut-off to establish the diagnosis and never needed medication. She came to our hospital for the first obstetric consultation, with a fasting glycemia of 112 mg/dL on the first trimester blood analysis. As she had a body mass index (BMI) of 23.1 kg/m2 and heavy familial history of diabetes, a CGK test was requested, which confirmed the diagnosis of MODY. During pregnancy, she kept reasonable control of blood glucose levels with diet and physical exercise alone. She had spontaneous labor at 37 weeks, but due to labor arrest, a cesarean section was performed, with the birth of a male newborn, 3590g (93rd percentile). ***Conclusion:*** Monogenic causes of diabetes, such as MODY, represent only a small fraction of cases. Nevertheless, our case highlights the importance of taking this hypothesis into consideration, especially when presented with young women with low to normal BMI, a history of hyperglycemia, and a family history of diabetes. This diagnosis is important as the therapeutic approach and possible complications during pregnancy are utterly different from the ones known in gestational diabetes.

URATE AND OTHER BIOCHEMICAL MARKERS AS PROGNOSTIC INDICATORS OF ADVERSE MATERNAL OUTCOMES IN PREECLAMPTIC WOMEN: A RETROSPECTIVE COHORT STUDY

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Problem statement: To explore if elevated serum urate and other biochemical marker levels (Calcium, AST, ALT) in preeclamptic women in early pregnancy (20 weeks gestation) are useful prognostic indicators of adverse maternal outcomes and to establish a predictive threshold value that indicates an increased risk of maternal complications. ***Methods:*** A retrospective cohort study was conducted at Gold Coast University Hospital, Australia involving 105 pregnant women with pre-eclampsia between January 2019 to December 2020. Preeclampsia was diagnosed based on local hospital guidelines. Serum levels

of urate, calcium, AST and ALT were extracted from the initial blood tests performed at booking visit prior to 20 weeks gestation. Maternal outcomes included post-partum haemorrhage, perineal tears, instrumental delivery, emergency caesarean section, placental abruption, blood transfusion requirements and ICU admission. ***Results:*** There were 105 women enrolled in this study. Serum uric acid at cut off 0.255 mmol/L was found to be a statistically significant predictor of general maternal complications such as post-partum haemorrhage, perineal tears, instrumental delivery, emergency c/s, placental abruption, blood transfusion requirements and ICU admission (AUC 0.625, P=0.032) with a 52.3% sensitivity and 72.5% specificity. Women with high urate levels at booking visit are 2.9 times more likely to experience an adverse outcome (OR 2.89, 95% CI 1.24,6.75; P = 0.014). Specifically, these women are 2.4 times more likely to experience a PPH (OR 2.4, 95% CI 1.05, 5.50; P= 0.038) and 2.5 times more likely to have an emergency caesarean section (OR 2.5, 95% CI 1.13, 5.54; P = 0.024). High serum calcium, AST and ALT at booking did not reveal a significant association with adverse maternal outcomes in women with preeclampsia (P 0.05). ***Conclusions:*** Maternal serum urate at booking has a potential role as a predictor of maternal outcomes in women with pre-eclampsia/severe pre-eclampsia and may play a role in establishing a global increase in risk but a larger cohort study is required to validate its reliability.

LOW BACK PAIN IN PREGNANCY: A DIAGNOSTIC AND CLINICAL APPROACH CHALLENGE

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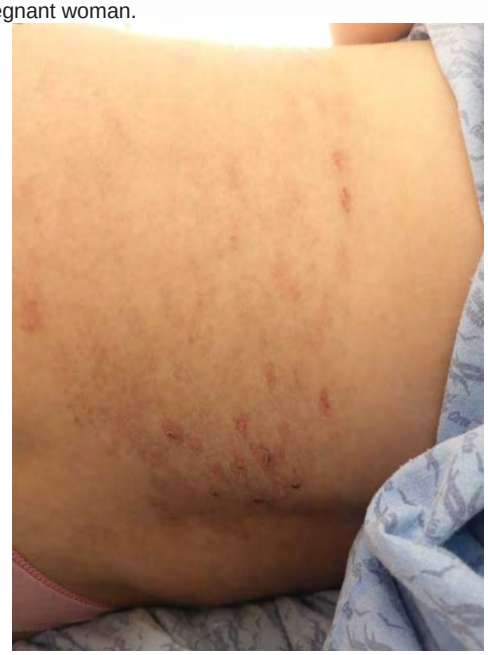
Problem statement: Low back pain is a very frequent complaint in pregnancy. In most cases is associated with musculoskeletal pathology or uterine contractility. Nevertheless, low back pain could be associated with rarer situations, such as neuropathic pain due to zoster infection. ***Methods:*** Description of a clinical case based on the clinical process ***Results:*** A 40-year-old woman, 30 weeks and 3 days pregnant, with personal history of active systemic lupus medicated with immunosuppressants, was admitted in the emergency department due to an intense, constant, left lumbar back pain, since one week ago. Physical and gynecological exam was normal, except a doubtful Murphy's Signal on the left side. The obstetric ultrasound showed no changes and the cardiotocography recorded no contractions. Blood tests revealed no increase of inflammatory parameters and the urinalysis was negative. Renal ultrasound showed no changes, with no sign of nephrolithiasis. The pregnant woman was hospitalized due to uncontrolled pain with oral therapy and for further etiological investigation. During the hospital admission, the pain was reliving and was assumed in context of musculoskeletal pathology. She was discharged from the hospital with analgesic medication. Two days after discharge, at the high-risk pregnancy appointment, the pregnant woman mentioned lumbar pain resurgence, more located and intense, that gets worse at night. She also highlighted the arising of skin lesions at lumbar region. On physical examination she presented, at left thoraco-lumbar region, a cluster of blister-like herpetic lesions, with dermatomal distribution. It was admitted herpes zoster infection and the pregnant was medicated with oral valaciclovir. One week after suspending the antiviral therapy, she returned to the emergency department due to continued uncontrolled left lumbar pain. On observation, the herpetic skin lesions were on healing process. It was assumed neuropathic pain due to herpes zoster infection. The woman was hospitalized to be submitted to a peripheral nerve block, to avoid systemic analgesic medication. The procedure occurred without complications and caused a substantial decreasing of pain. The remaining pregnancy and childbirth were uneventful. ***Conclusion:*** This case illustrates a rare cause of low back pain in pregnancy and highlights the challenge of pain control in pregnant woman.



MATERNAL OBESITY AND GESTATIONAL DIABETES MELLITUS INFLUENCY ON ADVERSE PERINATAL OUTCOMES

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Problem statement: maternal obesity and gestational diabetes mellitus (GDM) are both conditions related to adverse perinatal outcomes. Nevertheless, there is a controversy on which of these morbidities most influences poor maternal-fetal prognosis. The aim of this study was to evaluate the influency of isolated and associated prepregnancy obesity and GDM on adverse perinatal outcomes. ***Methods:*** a retrospective cross-sectional observational study was done with postpartum women from a south Brazilian`s public maternity, between august and december 2020. An interview was held and an application form was filled out by single pregnant women aged 18 or over, without previous diabetes mellitus. Starting from body mass index – BMI (based on the first antenatal visit) and GDM screening (based on Pan American Health Organization – PAHO criteria), the sample was stratified in four groups: non-obese (BMI30kg/m2) without GDM – reference group, non-obese with GDM, obese (BMI≥30kg/m2) without GDM and obese with GDM. Preeclampsia, c-section, large for gestational age (LGA) newborn (NB) and NB admission to neonatal intensive care unit (NICU) were analysed by odds ratio (OR) computation, ajusted for confounding factors, adopting 95% confidence interval (CI) and p<0.05 statistically significant. ***Results:*** 1618 postpartum women were included. Obese non-GDM patients (233/14.40%) had high risk of preeclampsia (OR=2.16; CI:1.364-3.426; p=0.001), GDM non-obese women (190/11.74%) had high risk of c-section (OR=1.736; CI:1.136-2.652; p=0.011) and NB admission to NICU (OR=2.32; CI:1.265-4.261; p=0.007), while those with GDM and obesity (121/7.48%) had high risk of preeclampsia (OR=1.93; CI:1.074-3.484; p=0.028), c-section (OR=1.925; CI:1.124-3.298; p=0.017) and LGA NB (OR=1.81; CI:1.027-3.204; p=0.040) when compared with non-obese non-GDM

patients (1074/66.38%). ***Conclusion:*** like GDM, maternal obesity individually enhances the risk of adverse perinatal outcomes. Its association with GDM amplify these risks.

OFFSPRING BIRTHWEIGHT AND PLACENTAL WEIGHT – DOES THE TYPE OF DIABETES MATTER? A POPULATION-BASED STUDY OF 319 076 PREGNANCIES

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Problem statement: Our aim was to estimate the difference in birthweight and in placental weight in pregnancies with type 1 diabetes, type 2 diabetes and gestational diabetes as compared to pregnancies without diabetes. ***Methods:*** By using data from the Medical Birth Registry of Norway during the years 2009-2017, we included 319,076 singleton pregnancies with delivery after the 21th week of pregnancy. We used linear regression analyses to estimate the difference in birthweight and in placental weight in grams (g) in pregnancies with type 1 diabetes, type 2 diabetes, and gestational diabetes, using pregnancies without diabetes as the reference. Adjustments were made for pregnancy duration and pre-pregnancy body mass index. ***Results:*** In pregnancies without diabetes, mean crude birthweight was 3527g (SD 552g). The adjusted mean birthweight was 525g (95% CI 502g-548g) higher in pregnancies with type 1 diabetes compared to pregnancies without diabetes. In pregnancies with type 2 diabetes, and pregnancies with gestational diabetes, birthweight was 192g (95% CI 160g-223g) and 102g (95% CI 93g-110g) higher, respectively. Mean crude placental weight was 664g (SD 147g) in pregnancies without diabetes. Compared to pregnancies without diabetes, the adjusted mean placental weight was 109g (95% CI 101g-116g) higher in pregnancies with type 1 diabetes, 50g (95% CI 39g-60g) higher in pregnancies with type 2 diabetes, and 31g (95% CI 28g-34g) higher in pregnancies with gestational diabetes. ***Conclusion:*** The increase in birthweight and in placental weight associated with maternal diabetes was most pronounced for type 1 diabetes, followed by type 2 diabetes, and gestational diabetes.

Disclosure of interest: *None*

LATERAL SINUS THROMBOSIS – A RARE POSTPARTUM COMPLICATION

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Problem statement: Cerebral Venous Thrombosis (CVT) is a rare cause of cerebral ischemia, corresponding to approximately 0.5% of stroke cases. CVT usually appears in the venous sinuses, which includes the lateral venous sinus. Among the risk factors associated with CVT, the puerperium is a phase in which thrombotic risk is particularly increased. The present work aims to describe the clinical case of a postpartum woman who, in the early postpartum period, was diagnosed with lateral sinus venous thrombosis. ***Methods:*** It is a case report of a puerperal woman with a rare postpartum complication. ***Results:*** This is a postpartum woman who underwent a cesarean section due to twin pregnancy with fetus 1 in breech presentation. On the first day postpartum, she started to experiencing intense temporal headaches associated with cervical rigidity. Computerized tomography and cranioencephalic nuclear magnetic resonance were performed, demonstrating subarachnoid haemorrhage and thrombosis of the lateral venous sinus. Anticoagulant therapy was initiated during hospitalization and the patient was discharged on the sixth postpartum day. During the puerperium, she returned to the hospital due to vaginal haemorrhage and underwent ultrasound-guided uterine curettage. ***Conclusion:*** The present clinical case documents a rare postpartum complication and how it was managed in order to have a favourable outcome.

No conflict of interest to declare.

GYNECOLOGICAL ONCOLOGY

EMBRYONAL RHABDOMYOSARCOMA (ERMS) IN A 15-YEAR-OLD GIRL WITH RECURRENT CERVICAL MASS: A CASE REPORT

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Problem statement: Embryonal rhabdomyosarcoma (ERMS) of the female genital tract is a rare malignant tumor. The overlapping clinical, radiological and microscopic features make it more difficult to accurately diagnose the disease, especially in resource-limited settings. Due to the rarity of this tumor, there is limited literature on the optimal management and treatment. ***Method:*** We report a rare case of a 15-year-old girl referred to our institution with an enlarging mass protruding through her vagina associated with abnormal vaginal discharge. She had normal menstrual cycles and her past medical history was unremarkable. An examination revealed a protruding mass through the vaginal introitus, thought to be arising from her cervix measured 20 x 15 cm in size. She underwent surgery to remove the mass. Histopathological features prompted initial diagnosis of angiomyofibroblastoma (AMFB). However, she was lost to follow-up until she represented after several months with recurrent excessive growth of the mass. A contrast-enhanced computed tomography (CT) of abdomen and pelvis confirmed the presence of inhomogen amorphous irregular lesion located at her vagina, which measured approximately 17,23 cm in its widest dimensions, without evidence of metastatic disease. All other measurements were normal. Discussions in a multidisciplinary meeting has been held, she was subsequently underwent total resection of the recurrent mass. ***Result:*** Total resection of the mass has performed. There was a grossly huge cervical mass protruding into vagina with surface irregularities measuring 20.5 x 13.5 x 3.7 cm. Histopathological analysis of the hematoxylin and eosin stained material showed spindle-shaped cells with hyperchromatic nuclei and eosinophilic cytoplasm. Immunohistochemically, the neoplastic cells were positive for desmin, myogenin, Myo-D1 and Ki-67. A diagnosis of ERMS was confirmed by an expert pathology consultant. ***Conclusion:*** The presence of a protruding mass from the genital tract in adolescents is a gynecological peculiarity and may constitute a malignancy. The difficulty in diagnosing ERMS and other mimics is related to the management and residual of different clinical symptoms. Accuracy of diagnosis in the early stages of the disease is a very favorable prognostic factor, especially in young patients.

CARING FOR PREGNANT WOMEN WITH CANCER: CHALLENGES FOR MIDWIVES

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Problem statement: Cancer cases during pregnancy are ever more common, possibly due to cellular deterioration associated with maternity at advanced ages and/or exposure to environmental risk factors. When coupled with

pregnancy, cancer can raise complex dilemmas, both ethical and therapeutical. It is urgent to attend to women going through these contradictory experiences: pregnancy and cancer. Multidisciplinary care is both a complementary and fundamental resource, with the importance of teamwork at the core of healthcare for women and their respective families when going through this simultaneous experience. Objective: Understand nursing strategies to provide speciality care to pregnant women with cancer. ***Methods:*** We developed a descriptive study with a qualitative approach to answer the question "Which strategies should allow a specialist nurse employ when dealing with pregnant women with cancer?". Semi directive interviews were the primary data collection method, with four interviews being conducted with obstetric specialist nurses from the Lisbon area having previous experience in caring for pregnant cancer patients between October 2019 and March 2020. The results were analysed using the WebQDA® software. ***Results:*** The scientific evidence on this subject are scarce. When promoting adaptative behaviour from pregnant women with cancer, specialist nurses consider communication and collaboration with other health professionals as their most relevant strategies—personal care limitations impact how healthcare is provided, with the need to adapt procedures to each patient. ***Conclusion:*** Investing in nurse training, with specific knowledge on caring with pregnant cancer patients, is a fundamental step towards multidisciplinary teamwork relevance, upheaving the importance of meetings with nurses from different teams and specific research on this topic.

Keywords: Nurse-Midwives; strategies; caring; pregnant women; cancer

GESTATIONAL TROPHOBLASTIC DISEASE IN PERIMENOPAUSAL WOMEN: A REPORT OF 2 CASES

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Introduction*:* Extreme reproductive ages are risk factors for gestational trophoblastic disease(GTD),and this is especially true for complete hydatidiform mole(CHM).Molar pregnancies are premalignant conditions that can progress to gestational trophoblastic neoplasias (GTN),such as invasive mole. ***Case 1:*** 54years-old perimenopausal woman with irregular menstrual cycles and no contraception method(CM), presented to a medical appointment for voluntary termination of pregnancy after a positive pregnancy test. Pelvic ultrasound(PUS) showed an enlarged uterus with endometrial thickening(ET) of 44mm with vesicular pattern and hCG level was 249.266mUI/ml.Chest x-ray was normal. A suction curettage was made and histopathological(HP) analysis confirmed CHM diagnostic. After an initial decrease in hCG levels, an increase in three consecutive weekly determinations was seen and the patient was sent to an oncology center. The patient was treated with methotrexate (MTX) with remission of the disease.***Case2:*** 56 years-old woman with no CM presented with irregular vaginal blood losses in the last 3 months and endometrial thickening of 42mm with cystic areas and was proposed to diagnostic hysteroscopy. Few days after, she went to the urgency room with increased blood losses and expelled a bulky vesicular mass through the vagina, whose HP analysis confirmed CHM diagnostic. Initial hCG level was 89.200mUI/ml. Chest x-ray showed some opacities and CT scan identified 4 infracentimetric pulmonar nodules and then the patient was sent to an oncology center. Chemotherapy with MTX was started with good initial response (reduction of volume/number of pulmonary lesions).Simultaneously, the patient was diagnosed with a synchronous colorectal cancer(CRC) which raised doubts about the origin of the secondary lung lesions. A laparoscopic right hemicolectomy was made and HP staging revealed a pT2N0 CRC. This way, the medical team concluded that the pulmonary lesions probably were CHM metastasis and the patient returned to the oncology center to continue staging and chemotherapy. ***Discussion:*** CHM has a high malignant potential(15%) and invasive mole is preceded by CHM in almost 95% of cases. Thus, clinical and serum hCG levels follow-up is very important after HP confirmation of molar pregnancy. Chemotherapy is very effective but hysterectomy could be necessary in cases of life-threatening bleeding. This 2 cases in perimenopausal women showed the importance of effective contraception method in order to prevent undesired or complicated forms of pregnancy.

ASSESSMENT OF MUCIN-GENERATED ANTI-CARBOHYDRATE ANTIBODIES CROSS - BINDING TO HUMAN CHORIONIC GONADOTROPIN (hCG) AND ITS SUBUNITS

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Problem statement: Recently we have shown, that majority of patients with ovarian cyst, but not those with ovarian carcinoma have significantly elevated levels of naturally-occurring serum antibodies of IgG isotype against human chorionic gonadotropin (hCG) and its subunits. In non-pregnant individuals elevated levels of hCG are associated with ovarian malignancy playing a role of a growth factor. Assessment of the subclass distribution revealed overwhelming prevalence of IgG2 class, indicating their anti-carbohydrate specificity. We propose, that these naturally-occurring antibodies are cross-reacting with hCG and its subunits through their sugar chains, and are elicited against oligosaccharides of blood group mucins produced by the ovarian cysts. ***Methods:*** We chose four commercial antibodies that are produced in response of ovarian cyst mucins and assessed their binding ability to the whole hCGαβ and its subunits - hCGβ, hCGα, hCGβ C-terminal peptide (hCGβCTP), and hCGβ core fragment (hCGβCF) by a standard enzyme-linked immunosorbent assay (ELISA). These antibodies were specific for the following antigens: SPM522 (Novus biologicals) - to Lewis A Blood Group Antigen; ab212418 (Abcam) to Blood Group Antigen Precursor; ab3968 (Abcam) - to Lewis B Blood Group Antigen; SPM297 (Novus biologicals) - to MUC5AC mucin. All antibodies were used in serial dilutions from 2 μg/ml to 62.5 ng/ml in PBS. ***Results:*** ab212418 (Abcam) monoclonal antibody which binds to carbohydrate determinante - Gal1-3GalNAc-R, showed significant cross-binding to hCGαβ, hCGβ, hCGα and hCGβCTP. Interestingly, this antibody did not bind to hCGβCF (Figure 1).

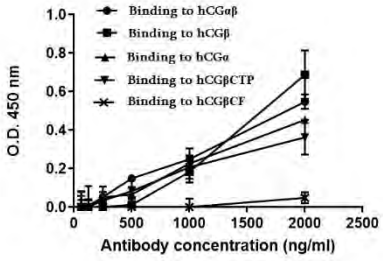

Figure 1: Binding of different concentration of monoclonal antibody ab212418 (Abcam) to hCG and its subunits assessed by ELISA. The other tested antibodies did not show appreciable cross-binding. Our data is the first

indication that Gal1-3GalNAc – a structural component of mucins released by an ovarian cyst generates an antibody cross-binding to hCG and its component potentially providing protection from hCG tumour growth factor. ***Conclusion:*** Further studies for identification and characterization of a carbohydrate determinant(s) which generates cross-binding antibodies to hCG are important as a basis for anti-tumour molecular therapies and vaccine development.

SPONTANEOUS UTERINE RUPTURE BY TUMOR

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Problem statement: Uterine leiomyosarcoma is a rare uterine malignancy that arises from the smooth muscle of the uterine wall. Compared with other types of uterine cancers is an aggressive tumor associated with a high risk of recurrence and death, regardless of stage at presentation. ***Case report:*** 85-year-old woman with a medical history of hypertension, ischemic stroke, and varicose ulcer of the left lower limb. The patient was admitted to the Emergency Department with the following complaints: abdominal pain and obstipation for 2 days, she also reported asthenia, without associated weight loss. On physical examination, the abdomen was distended, tympanized, and painful on superficial and deep palpation, more intense in the left quadrants. TAC-TAP was requested, which revealed "... a structure that is attributed to the uterus, which is distended with heterogeneous content and gas that suggests the presence of abundant pus. It also shows rupture of the left uterine wall at the level of the fundus with an adjacent collection, with an abscessed appearance, with about 63 mm in diameter. There is another small abscessed collection at the pouch of Douglas. There is also an abundant pneumoperitoneum with a large amount of gas near the anterior abdominal wall that also extends to the upper abdomen." It was proposed an exploratory laparotomy with the collaboration of General Surgery and Gynecology. A median laparotomy was performed. A large left pelvic abscess was found, originating from the uterine rupture. The uterine cavity was filled with 3 tumor fragments and necrosis. The tumor was also infiltrating the posterior wall of the bladder, the left pelvic wall, and the sigmoid, making it unresectable. There was no evidence of liver or peritoneal metastasis. The peritoneal cavity, which contained pus in all quadrants, was abundantly washed and, due to the impossibility of tumor resection, the uterus was left under ample drainage. ***Conclusion:*** One plausible diagnostic is a Uterine leiomyosarcoma extending beyond the uterus to the bladder, the pelvic wall and the sigmoid, with additional purulent peritonitis and abdominal sepsis. For women with the extrauterine disease, the role of surgery is controversial.
I have no conflict of interest.

ENDOMETRIAL ADENOCARCINOMA IN A 36 YEAR OLD: A CASE REPORT

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Introduction: Endometrial carcinoma commonly presents in post-menopausal women with abnormal vaginal bleeding. Postmenopausal women comprise 75-80% cases of endometrial carcinoma, with only about 1–8% occuring in women less than 40 years. We report a case of endometrioid adenocarcinoma diagnosed in a 36year old during her investigation for infertility. Endometrial cancer in the young is most often overlooked and diagnosis poses a challenge in management in these women most of whom wish to preserve their fertility. ***Case report:*** A 36year old nulliparous woman was referred for investigations of infertility. She was overweight (BMI=52.1), with a history of polycystic ovaries. Transvaginal ultrasound showed an endometrial lesion suggestive of polyp. Based on these imaging findings and in view that she was going to start stimulation in IVF cycle, she was considered for hysteroscopy, dilatation and curettage and resection of endometrial lesion. During hysteroscopy a polypoidal area was noted, so direct resection of this area was carried out. Endometrial sampling was also sent for further examination. The pathology report showed foci of complex hyperplasia in the endometrial polyps and moderately differentiated endometrioid endometrial carcinoma in the endometrial curettings. In order to determine staging, a CT chest/abdomen/pelvis and pelvis MRI were carried out. There was no evidence of lymphadenopathy or metastatic disease on CT, while the result of pelvic MRI showed the lesion confined to the uterus with less than 50% myometrial invasion. Management posed a dilemma considering her age and fertility status. Case was discussed at the multidisciplinary meeting and patient was counseled regarding the management. Staging laparotomy was done with total hysterectomy with bilateral salpingo-oophorectomy. Surgicopathological findings were in keeping with stage 1A according to the International Federation of Gynaecology and Obstetrics (FIGO), 2000 classification of endometrial cancer. ***Conclusion:*** In the present case it was surprising to see endometrial carcinoma in the younger age group presenting incidentally as part of investigation for infertility. Unopposed estrogen conditions (high BMI, premenopausal anovulation in polycystic ovary syndrome and nulliparity) predispose to endometrial cancer. Endometrial cancer needs to be excluded whenever there are abnormal sonographic findings especially in presence of these risk factors irrespective of age.

COMPARISON OF CERVICAL CANCER PATIENT QUALITY OF LIFE AFTER RADIOTHERAPY AND CHEMOTHERAPY TREATMENT AT PROF DR R D KANDOU GENERAL HOSPITAL

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Problem statement: Cervical cancer is the second most common cancer among females in Indonesia. Radiation therapy and chemotherapy are the current recommended treatment modalities, if surgery is not the eligible option. There are several side effects which can occur when these treatments are initiated. The aim of this study is to compare the major symptoms of radiotherapy and chemotherapy in cervical cancer patients at Prof. Dr. R. D. Kandou General Hospital. ***Methods:*** The data was collected by interview, using EORTC QLQ-C 30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core module, consist of 30 question) and EORTC QLQ-CX 24 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Cervical Cancer module, consist of 24 question) in a cross sectional study within the period of May to July 2021. The quality of life between chemotherapy and radiotherapy patients was evaluated using the Man-Whitney U tests. ***Results:*** From 104 patients with cervical cancer whom had completed radiotherapy (n=75) or chemotherapy (n=29) regiments, major post-radiotherapy symptoms include: abdominal cramps (20%), anxiety (20%), need to rest (14.7%), pain (14.7%), finger numbness (13.3%), vaginal discharge (13.3%) and other complaints (4%). On the contrary, major post-chemotherapy symptoms include: lack of appetite (34.5%), pain (31%), anxiety (24.1%), nausea

(3.4 %), vomiting (3.4%) and others complaints (3,6%). The quality of life evaluation shows that there is a significant difference between chemotherapy and radiotherapy treatments (asymp value. sig. 2-tailed 0.01 0.05). ***Conclusion:*** There is a significant difference in major post-chemotherapy and radiotherapy symptoms. Patients treated with chemotherapy or radiotherapy must be informed the symptoms severity and some potential efforts should be made to treat the symptoms. Consequently, the majority of patients diagnosed with cervical cancer have decrease in sexual desire to have intercourse with their partner. It is imperative to pay attention and monitoring these symptoms during follow-up phases and to provide the most adequate approach in management planning, in order to improve the quality of life.

Keywords: Cervical Cancer, Quality of Life, Radiotherapy, Chemotherapy.

Disclosure of interest: The authors declared no conflict of interest in this study.

GYNECOLOGY

FIRST IN WOMEN USE OF ASPIVIX TM, AN ATRAUMATIC INNOVATIVE UTERINE CERVICAL TRACTION DEVICE: A PILOT STUDY

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Alignment of uterine cervix with vaginal canal is often required during intrauterine contraceptive device (IUD) insertion. The standard of Care - the tenacula, could cause pain, bleeding therefore representing an obstacle for patients to pursue this contraceptive. Aspivix™ is a new device, designed to deliver atraumatic cervical traction via sucction technology while respecting the semi-circular anatomical shape of the cervix. The pilot study is single arm non-comparative to assess the usability, the safety and the efficacy of the device in a minimum of 10 women received IUD using this atraumatic device. We prospectively collected the device efficacy (ability to insert IUD with Aspivix™ device alone without recourse to conventional tenaculum), usability (number of placements attempts before traction can be applied, number of spontaneous releases), safety (adverse events, cervical bleeding and ecchymosis), patient-reported pain scores at specific time points during IUD insertion procedure and patient satisfaction.13 participants were included. 11 participants had a successful IUD insertion, 7 with Aspivix TM device alone (54%) and 4 after switch to standard single tooth tenaculum. 2 out of 13 participants (15%) experienced IUD insertion failure irrespective of the device used – Aspivix and tenaculum - due to cervical stenosis. The usability of the device was satisfactory in 77%. In 9 out of 13 cases, the practitioner reported spontaneous releases of the device from the grasped tissue. No bleeding or only limited ecchymosis were caused by the Aspivix™ device. No adverse events were reported. Participants reported almost no pain while the Aspivix ™ device was applied. The participants, who had the IUD insertion achieved with Aspivix device alone strongly agreed that they were overall satisfied with the procedure. The Aspivix device can be used to hold and manipulate the cervix during IUD insertion with efficacy, safety, and usability. Characteristics of the device that are appreciated by the practitioners included the lack of pain, absence of trauma to the cervix, maneuverability, and ease of use. Its use requires a short learning curve to avoid releases. With the results of this pilot study, a comparative study with the standard single tooth tenaculum will be performed.

VULVAR CONDYLOMATOSIS. NEW LOCAL SYNERGISTIC TREATMENTS.

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Condylomata acuminata or Genital Warts are the clinical expression of infection by certain types of human papillomavirus (HPV) considered low oncogenic risk (No. 6 and 11). Currently,they are considered one of the most frequent sexually transmitted diseases with an increasing incidence in most populations. There are multiple forms of presentation and extension of the lesions (from very localized forms with a low volume of disease or very extensive tract). **The clinical case** is a young woman, 26-year-old patient who came to our office at CIMEG MADRID in August 2020 presenting multiple vulvar condylomatous lesions previously evaluated and treated in a dermatological center with local cryotherapy and sinecatechin (veregen) ointment 2 times a day at home; she decides to seek another medical opinion.
Ethnicity: Latin American.
Personal pathological history: no chronic diseases.
Smoker: Yes (3-5 cigarettes a day).
First sexual relations: 16 years.
No. of sexual partners : 4
Previous pregnancies: No.
Contraceptive method: No
Provides cervical cytology: benign changes in june 2020.
In our unit, after adequate physical and colposcopic examination we decided to start local therapy with **ErYag Laser** (Fotona laser) with a wavelength of 2940nm together with Local Vulvar **Papilocare Ge**l as an adjunct to local laser therapy, to help re-epithelialize and hydrate the area due to the composition of the gel like for example: Hyaluronic acid niosome providing hydration and elasticity. Coriolus Versicolor: re-epithelializes genital lesions Antioxidant beta-glucan niosome to maintain an adequate skin and mucosa structure and Healing and repairing Centella Asiatica phytosomes, etc. **The combination or synergy of Laser Therapy with Papilocare vulvar local gel**; It was suitable for this patient with a satisfactory evolution with total elimination of the lesions and absence of recurrences 6 months after treatment. (iconography, before and after treatment). Sometimes, the absence of a single effective therapy for all patients forces us to individualize when choosing between the different available procedures (excisional, destructive, topical, etc.). The nature of the disease, and the fact that it is linked to sexual transmission, cause a great physical, emotional and psycho-sexual impact among affected patients, so we must insist on the adolescent population to comply vaccination.

ARGON PLASMA COAGULATION FOR MANAGEMENT OF PERSISTENT VAGINAL BLEEDING IN POSTMENOPAUSAL WOMAN WITH VAGINAL PESSARY: A CASE REPORT

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Problem statement: Ring pessaries are commonly considered as a non-surgical treatment for Pelvic Organ prPolapse (POP) in elderly women with prolapse symptoms as bulging, pelvic pressure and voiding or urinary difficulty. Most of the patients referred to be comfortable with this device. One of the problems with pessary use in long-term users is the vaginal bleeding specially in women with severe genital atrophy. In these cases, removing the pessary for two weeks and topic estrogens applications are required. In rare cases the bleeding cannot be stopped. ***Methods and Results:*** Description of a case report of an

82 year old woman with a persistent vaginal bleeding because of vaginal erosions caused by her pessary. She had a personal history of abdominal hysterectomy and vaginal vault during the last 14 years. She also had the risk factor of severe vaginal atrophy and her chronic anticoagulation treatment. The pessary was removed and silver nitrate on the vaginal surface was applied. Despite the vaginal tamponade the woman continued bleeding. In the end, the bleeding was successfully managed using Argon Plasma Coagulation (APC) directly on the surface of the vaginal mucosa. ***Conclusion:*** Argon Plasma Coagulation (APC) is an electrosurgical thermal ablation technique used to achieve hemostasis in bleeding. This technique has been described as a good alternative for digestive ulcers, digestive bleeding tumors and also in hemoptysis. The APC induces immediate resolution of bleeding with long-term effectiveness. It is a safe, cheap and easy technique for acute haemorrage. The Argon Plasma Coagulation can be considered as an optimal treatment for persistent vaginal bleeding in women pessary users.

The author declares no conflict of interest in this article.

TRAUMATIC CLOACA AFTER COMPLICATED VAGINAL DELIVERY: A CASE REPORT

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Problem statement: To assess the anatomic and functional results of surgical treatment of traumatic cloaca after reconstructive surgery of the perineal body and rectovaginal septum using the puborectal and external sphincter muscles. ***Method:*** A clinical case of a 70- year-old woman submitted to surgical treatment for correction of the cloaca. Physical examination, diagnostic tests, symptoms and Quality of life score were completed before and 6 months after surgery. ***Results:*** Traumatic cloaca is a severe obstetric complication characterized by an anatomic deformity of the anus and vagina caused by the severe damage of the sphincter and perineal body. We describe the anatomic and functional outcomes after reparation of a traumatic cloaca which had occurred 33 years earlier after seven vaginal deliveries at her home. The patient had an open rectovaginal communication with a large anterior sphincter defect and fecal incontinence. The patient had a complete disruption of the perineum, anal canal, short length vagina, and rectum, with a mean internal and external sphincter defect of 195 degrees. Those suffering from a cloaca have severe fecal incontinence and symptoms similar to a rectovaginal fistula because of the lack of the distal rectovaginal septum. Consequently, the woman suffered from grave perineal skin irritation and recurrent vaginal and urinary tract infections. Furthermore, absence of sexual activity or dyspareunia leads her to social isolation, alterations in the body image, depression and a poor quality of life. The surgery performed in this case was a CORMAN technique and sphincteroplasty. Anatomic recovery and fecal continence restoration have been accomplished completely by a follow-up at 6 months. Preoperative Fecal Incontinence Wexner Score was 20 and postoperative was 6 Also the Epidemiology of Prolapse and Incontinence Questionnaire-EPIQ showed the clinical improvement. ***Conclusion:*** The layered repair of the anovaginal structures including internal and external sphincteroplasties is an optimal technique for treating a cloaca deformity and restores the anatomy, the sexual activity and the urofecal functions with low rates of complications and excellent quality of life score.

The author declares no conflict of interest in this article.

0.005% ESTRIOL VAGINAL GEL IN THE PREVENTION OF RECURRENT URINARY TRACT INFECTION AND ASSOCIATED OUTCOMES IN POSTMENOPAUSAL WOMEN

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Problem statement: Genitourinary Syndrome of Menopause (GSM) is associated with an increased rate of urinary tract infections (UTIs). In fact, it is estimated that the annual incidence of UTIs among women older than 50 years is around 9%. Topical estrogens such as 0.005% estriol vaginal gel show a clear benefit for relieving genital symptoms but the effect in prevention of UTIs is yet to determine. ***Methods:*** Postmenopausal women between 45 and 80 years with vaginal dryness and a history of recurrent UTI (rUTI: ≥ 2 in 6 months or ≥3 in 12 months) were eligible for this randomized, double-blind placebo-controlled study. Number and incidence rate of UTIs (based on clinical parameters and microbiological confirmation), asymptomatic bacteriuria, as well as vaginal pH, symptomatology, antibiotic use and tolerability were determined at baseline, 3, 6, 12, 18 and 24 weeks visits. Additionally, extra visits were performed when urinary symptoms appeared. ***Results:*** 108 women, 53 with estriol and 55 with placebo were included in the study. 50 µg estriol vaginal gel significantly reduced the incidence rate of urinary tract infection (per 100 person and year) by 26% as compared to placebo (0.32 vs 0.44, p0,0001). Accordingly, the incidence rate of asymptomatic bacteriuria was also significantly decreased (p=0.0469). These results were further sustained by the reduced need of non-programmed visits and the low antibiotic use in women that received estriol. Tolerability was comparable between treatment groups. All women considered treatment tolerability as good, very good or excellent at the end of the study. ***Conclusions:*** Ultra-low dose 0.005% estriol vaginal gel significantly reduced the incidence rate of both urinary tract infections and asymptomatic bacteriuria in postmenopausal women with rUTI, showing an overall benefit in clinical and microbiological results. Treatment with 50 µg estriol was also associated with favorable evidence regarding other relevant related clinical outcomes such as the need of additional consultations for UTI symptoms.

UTERINE FIBROIDS AND CLINICAL DECISION MAKING - WHEN SHOULD PELVIC MRI BE ORDERED?

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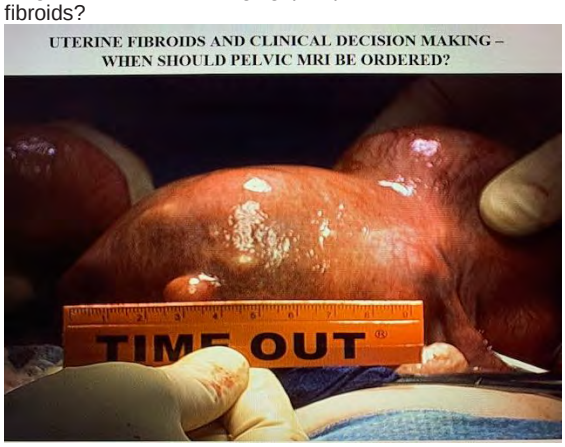
Background: Hysterectomies are the most common major gynecological surgeries performed worldwide. Indications for hysterectomy include uterine fibroids, abnormal uterine bleeding, chronic pelvic pain, uterine prolapse, and carcinoma of the endometrium or the cervix. The clinical decision to proceed with hysterectomy is made on a case-by-case basis and a shared decision making with the patient. ***Case Report:*** A 44-year-old woman presented to the hospital with vaginal bleeding, pelvic pain and dizziness. She had a 10-year history of passing large blood clots with menstruation lasting 7-10 days. Clinical examination showed morbidly obese cooperative lady, pale, anicteric and abdominal examination that was limited by body habitus. Laboratory evaluation showed hemoglobin of 6.2 gm with iron studies indicative or iron deficiency anemia aswell. Ultrasound of the pelvis revealed multiple leiomyomatous changes of the uterus with the largest discrete fibroid measuring 8.5x8.5 x11.2cm. She was admitted into the hospital, received blood transfusion and endometrial biopsy that showed no endometrial hyperplasia. She was discharged home on oral iron supplementation. At follow up appointment, after extensive

discussion regarding her options and alternatives, she had no desire for more children and chose to have hysterectomy. She had two previous cesarean sections - relative contraindication to endometrial ablation, moreover, endometrial ablation may not be appropriate treatment for multiple fibroids. She was prescribed Leuprolide 3.5 mg monthly for 3 months in an attempt to shrink the fibroids. Informed/signed consent on chart for robotic-assisted hysterectomy with bilateral salpingo-oopherectomy (BSO) on chart. At time of surgery the uterus measured over 22-weeks size with multiple fibroids. Surgery was converted to total abdominal hysterectomy with BSO due to uterine size, pelvic adhesions and endometriosis. Her postoperative course was uncomplicated. ***Discussion:*** There are other options for management of uterine fibroids such as uterine artery embolization (UAE), focused ultrasound surgery (FUS) however, she chose hysterectomy. Evaluation of patients with fibroid can be challenging especially in the morbidly obese patient. She had pelvic ultrasound that gave impression of a 12 to 14-week size uterus but turned out to be over 22-weeks in size. Therefore, when should pelvic magnetic resonance imaging (MRI) be ordered for uterine fibroids?



EFFICACY AND SAFETY OF THE ERBIUM YAG SMOOTH® VS. LESS INVASIVE SURGERY IN THE TREATMENT OF URINARY INCIONTINENCE IN WOMEN

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Noninvasive solutions, as behavioral treatments, pelvic floor muscle training and functional electrostimulation of the pelvic floor (FES) are recommended as first-line management strategies for (stress) urinary incontinence (S(UI) in women. Less invasive mesh techniques are relatively effective, but are not immune to complications such as bleeding, bladder perforation, urethral injury, infection, and the retention requiring mesh resection. In patients for whom the risks of anesthesia and surgery are too high, a minimally invasive approach with shorter recovery times and lower implicated costs is recommended. In this sense, recent evidence supports laser treatment as an alternative and effective intervention for SUI. Since 2015 many clinical studies have shown the advantages of different energy-based devices (EBD) for the treatment of SUI/genitourinary syndrome of menopause (GSM). Most studies have referred to the use of nonablative Er:YAG SMOOTH® laser for the treatment of SUI and mixed urinary incontinence (MUI), and both Er:YAG and CO2 lasers in the treatment of GSM. Head to head studies showed that Er:YAG SMOOTH® therapy improve urinary incontinence in women as effectively as the tension-free vaginal tape (TVT) and transobturator tape (TOT) procedures. For patients with mixed urinary incontinence (MUI), some in the TVT and TOT groups showed exacerbation. However, all patients in the laser therapy group tended to improve. Vaginal erbium laser (VEL) safely and effectively improve overactive bladder symptoms score (OABSS) compared to common pharmacotherapies, anticholinergics and β3-adrenoceptor agonists, however through a different mechanism. VEL improves blood flow in the bladder, urethra, and vaginal wall reducing OABSS without adverse effects typical for medication. Comparative study showed that Er:YAG SMOOTH® deliver equal significant reduction in SUI, both in hysterectomized and non-hysterectomized patients. For achieving efficacy and safety it is important to follow proper protocol. However, prospective randomized placebo controlled trials are needed with a larger number of participants in order to assess the effectiveness of laser treatment in SUI symptoms with a longer follow-up period.

ASYMPTOMATIC MICROPERFORATED TRANSVERSE VAGINAL SEPTUM

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Problem statement: Transverse vaginal septum is a rare type of Mullerian anomaly with an incidence of 1 out of 70,000 females. It results from failure of the canalization of the vaginal plate to the point where the urogenital sinus meets the mullerian duct and usually presents at menarche with symptoms of outflow tract obstruction. Patients with a perforated septum often have normal menses and usually present with difficulties with intercourse or infertility. ***Methods:*** We present a case report of a 27-year-old woman with an asymptomatic perforated transverse septum who underwent surgical treatment. ***Results:*** 27-year-old nulliparous woman attended the gynecology for a routine assessment. She reported regular menstrual cycle 3-4/30 days, changing 2-3 pads per day, and no history of clots or dysmenorrhea. On examination there was a blind vagina with a pin hole opening in the center (2-3mm). Based on clinical examination finding, a provisional diagnosis of transverse vaginal septum was made. Transvaginal ultrasound showed haematocolpos, normal uterus, cervix and ovaries. MRI showed a thin low signal intensity structure in T2W image, measuring a thickness of 7.5mm which is 3cm from the introitus with a small fenestration. Proximal and midportion of the vagina appeared normal. The surgery was planned with hysteroscopy support. Has been viewed a septum with a small hole with menstrual blood flowing out. The septum was sectioned transversely, opened with a 5fr bipolar electrode and then completely excised circumferentially by electrosurgery. Application of hyaluronic acid was prescribed to prevent the risk of stenosis, and an early return to sexual activity was recommended. Post-operative recovery was good and uneventful and the vagina healed well without stricture formation. ***Conclusion:*** Imperforate obstructive vaginal malformations can be easily diagnosed and may be likely to cause retrograde menstruation, which in turn impedes outflow of menstruation and leads to hematocolpometra and amenorrhea. In the present case, the septum was located at the upper part of the vagina and the couple had no complaint of coital quality. The patient also had no complaints of dysmenorrhea or amenorrhea, possibly owing to incomplete obstruction of the vagina. In our case, the vaginoscopic approach using a hysteroscope for the septum recection is available, feasible, convenient, and effective tool.

THE EFFICACY OF LOCAL TRANEXAMIC ACID USE IN BLEEDING MANAGEMENT OF MYOMA UTERI SURGERY: A SINGLE-CENTER PROSPECTIVE STUDY

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Problem statement: Per-operative bleeding is one of the major problems that can be seen during myomectomy surgery. In cases of severe bleeding, hysterectomy may be indicated to maintain bleeding control. It is aimed to reveal the effectiveness of local tranexamic acid (TA) use in bleeding control of myoma uteri surgery. ***Methods:*** Patients scheduled for open surgery with the diagnosis of myoma uteri between 2017 and 2019 were included in the present study. As a prospectively designed analysis, the test group(n=19) who underwent myomectomy with local TA application was compared with the control group(n=20) who received myomectomy without local TA application in terms of demographic characteristics of the patients, clinical findings (laboratory measurements, per-operative bleeding, blood transfusions, length of hospital stay, complication rates). Patients with a history of hysterectomy and the ones who were operated for malignancy were not considered for evaluation. ***Results:*** Thirty-nine patients were included in the study. The calculated mean age was 39.95 years (Test group: 40, control group: 39.9). Per-operative average transfusion rate was 5.3% in the test group and 5% in the control group. The average length of stay was similar for both groups (p=0.183; p0.05 (Test group: 1.42±0.51, control group:1.7±0.66)). There was no statistically significant difference between the two groups in terms of operation lengths (p=0.409; p0.05 (Test group: 44.37±9.06, control group: 46.8±9.13)). The use of transamine didn't provide significant benefit in terms of bleeding compared to the control group (p=0.899;p0.05). ***Conclusion:*** This is the first study in relevant literature evaluating local TA use in myomectomy surgery. Local TA use in myomectomy surgery has provided no clinical benefit in terms of bleeding control.

Disclosure statement: *None declared.*

ACUTE NON-PUERPERAL UTERINE INVERSION DUE TO MYOMA GEBURT : A RARE CASE REPORT

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Problem statement: The purpose of this case report is to know how to diagnose and treat acute non-puerperal uterine inversion due to myoma geburt. ***Methods:*** Case report. ***Results:*** A 43-year-old nullipara, came to the hospital for vaginal bleeding in the past 5 hours. Since 2 months ago she recurrently experienced this complaint. She had been complaining a big mass in her vagina since 2 months ago which revealed 5 hours before admission. The significant physical findings was a mass revealed from vagina sized 23 x 15 cm, smooth surface with pus and necrotic tissue, firm consistency, well demarcated, protruding from the vaginal introitus. The cervix can`t be evaluated. We performed a transvaginal uterine excision, repositioned after removing the mass. The surgery uncovered a mass size 23 x 15 cm, which was one of the largest mass that have been reported. The pathology examination result is leiomyoma uterine with hyalinosis. The patient was examined 1 week and 3 months after the surgical procedure, from gynecology examination the inspection was normal, there is no blood or fluor, smooth cervix with closed ostium external of uterus. ***Conclusion:*** Initial assessment and resuscitation would be the priority as some patients may be in septic or in hemorrhagic shock, followed by correction of anemia, pain relief, and starting antibiotics. The type and approach of surgery should be individualized considering the age, desire for future fertility, etiology, and the stage of the disease in case of malignancy. In this case we performed a transvaginal uterine excision, repositioned after removing the mass. The final outcome of surgery is repositioning uterine into anatomy position. Non-puerperal uterine inversion is an exceptional and life-threatening disease that most gynaecologist will rarely encounter in their career. Careful examination will yield correct diagnosis and treatment that would help to decrease patient morbidity and mortality.

ASSESSMENT OF QUALITY OF LIFE IN WOMEN WITH MULTIPLE SCLEROSIS AND SEXUAL DYSFUNCTION

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Problem statement: Multiple sclerosis (MS) is often associated with sexual dysfunction, which increases due to disease progression. The first symptoms of MS occur at the age of 20 to 40 years, when sexual function (SF) is particularly important for patients, and sexual dysfunction can affect the realization of reproductive function and quality of life. Scientific studies report a significant (40 - 80%) prevalence of sexual dysfunction among women with MS, but at the same time insufficient attention of doctors to the diagnosis and treatment of sexual dysfunction. ***Methods:*** 98 women of reproductive age with a confirmed diagnosis of multiple sclerosis were examined. All study participants completed the MSQOL-54 (Multiple sclerosis quality of life questionnaire) and the sexual dysfunction questionnaire. The results of the questionnaire were evaluated on a scale, where the highest score corresponded to normal sexual function, and the lowest - to pronounced changes. According to the results of the survey, patients were divided into two groups: with a violation of SF and with normal SF and we compared the quality of life of women in both groups. ***Results:*** Sexual dysfunction was found in 76% of subjects, of whom 24% had severe changes. Among sexual disorders, the absence of sexual desire (39%) and less intense orgasms (27%) predominated. Women with MS reported dissatisfaction with their sex lives in 63% and deterioration in sexual function in 41% after being diagnosed with MS. Patients with MS in combination with sexual dysfunction showed a worse quality of life by 8.6 points compared with women without SF disorders. ***Conclusion:*** Due to the high prevalence and negative impact on quality of life, it is necessary to advise patients on the possibility of developing sexual dysfunction at the stage of establishing the MS diagnosis and to ensure further monitoring of SF for timely detection and correction of disorders.

THE BENEFICIAL EFFECT OF A COMBINATION OF SOY ISOFLAVONES, 8-PREGNYL-NARINGENINE (8-PN) AND MELATONIN FOR IMPROVING THE QUALITY OF LIFE OF POSTMENOPAUSAL WOMEN WITH HOT FLASHES.

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Problem statement: Vasomotor symptoms (VMS) negatively affect health-related quality of life (QoL) of peri-postmenopausal women. Phytoestrogens can exert favourable effects and alleviate hot flashes and other VMS in these women, however evidence to guide clinical recommendations is inconsistent. This study aims to demonstrate the effect of Flavia Nocta (a combination of 54mg of soy isoflavones –24.5mg genistein–, 100µg of 8-PN and 1mg of melatonin) on the QoL of postmenopausal women with hot flashes. ***Methods:*** Women with moderate to severe hot flashes (at least 5 daily or 35 weekly) were included in this multicentric, prospective, open-label study. All women received one capsule of Flavia Nocta every day over 12 weeks. Number and intensity of hot flashes were registered in a diary completed daily and evaluated at

baseline, 4 and 12 weeks of treatment. QoL was evaluated at same timepoints with the Menopause-specific QoL Questionnaire (MENQOL) –29 questions in 4 domains, range 1-8 each, 8 meaning worst-, and Cervantes Scale - 31 questions in 4 domains; global punctuation 0-155, 0 meaning worst-. Tolerability and acceptability were also assessed. ***Results:*** Forty women aged 53.4(5.1) years -mean(SD)- were included. After 12 weeks all MENQOL domains had significantly improved from baseline (p0.001): vasomotor 7.22(1.0) to 4.24(1.0); psychosocial 3.84(1.9) to 2.83(1.5); physical 4.93(1.6) to 3.71(1.4); and sexual 5.26(4.6) to 4.61(1.7); meaning improvements of 41%, 26%, 25% and 7%, respectively. Similarly, this favourable effect of Flavia Nocta over QoL was evidenced in the Cervantes Scale: significant improvements were shown in the global punctuation 77.21(26.0) to 51.63(26.2); menopause domain 46.8(12.9) to 29.4(14.9); and psychic domain 16.4(10.0) to 9.37(7.7); translating improvements of 35%, 39% and 52%, respectively (p0.001). ***Conclusions:*** 54mg of soy isoflavones -containing 24.5mg genistein-, 100µg of 8-PN and 1mg of melatonin shows a substantial and clinically significant effect for improving the quality of life of postmenopausal women with hot flashes. The important alleviation of vasomotor symptoms (hot flashes, nocturnal sweats, sleeping difficulties) produced by this combination may contribute to the improvements in the women's physical and psychosocial spheres which are essential for their well-being also in this period of their lives.

SOY ISOFLAVONES, 8-PREGNYL-NARINGENINE (8-PN) AND MELATONIN REDUCE HOT FLASHES IN POSTMENOPAUSAL WOMEN

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Problem statement: Hot flashes are the most common symptom of menopause and may persist for several years. They can affect quality of life (QoL), but also contribute to sleep and mood disturbances, which can potentially affect daily activities. The lack of acceptance of hormonal therapy due to concerns about its safety has led to popularization of alternative therapies. This study aims to demonstrate the effect of Flavia Nocta (a specific standardized extract of 54mg of soy isoflavones –24.5mg genistein–, 100µg of 8-pregnyl-naringenine and 1mg of melatonin) over hot flashes and the QoL of postmenopausal women. ***Methods:*** Postmenopausal women with moderate to severe hot flashes (at least 5 daily or 35 weekly) were included in this multicentric, prospective, open-label study. All women received one capsule of Flavia Nocta every day over 12 weeks. Number and intensity of hot flashes were registered in a diary completed daily and evaluated at baseline, 4 and 12 weeks (w) of treatment. QoL was evaluated at same timepoints with the Menopause-specific-QoL-Questionnaire (MENQOL) and Cervantes Scale. Tolerability, safety and acceptability were also assessed. ***Results:*** Forty women [age 53.4(5.1) years -mean (SD)-; BMI 25.27(3.49) kg/m2] were included. A significant decrease in the total number of weekly hot flashes was observed, from 65.34(19.9) at baseline to 43.25(30.0) at 4w (33% reduction; p0.0001) and 25.74(27.2) at 12w (60% reduction; p0.0001). Moderate and severe hot flashes were also significantly reduced, from 55.63(15.5) at baseline to 32.66(21.1) at 4w (38% reduction; p0.0001) and 13.47(15.8) at 12w (76% reduction; p0.0001). All four domains of MENQOL as well as the menopause, psychic, couple domains and global punctuation of the Cervantes Scale were significantly improved after 4 and 12w. No treatment-emergent adverse events occurred. Tolerability and acceptability were mostly considered very good or excellent by women. ***Conclusions:*** This study suggests that a standardized extract of 54mg of soy isoflavones –including 24.5mg of genistein–, 100µg of 8-pregnyl-naringenine and 1mg of melatonin is a well-tolerated nonhormone therapy that produces a rapid and substantial reduction of hot flashes associated with menopause. Moreover, this combination produces a clear improvement in the well-being and QoL of these mid-life women

POSTMENOPAUSAL BLEEDING AS A SYMPTOM OF ENDOMETRIAL ACTINOMYCOSIS IN THE ABSENCE OF INTRAUTERINE CONTRACEPTIVES AND WITH ALLERGY TO PENICILLIN

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This case study focuses on a 66-year-old patient, allergic to penicillin, with endometrial actinomycosis, with no history of intrauterine contraceptive (IUD) administration, with symptomatology in the form of postmenopausal uterine bleeding and lower pelvic pain. Endometrial actinomycosis is an infection that occurs rarely, accompanied by non-specific symptomatology. The diagnosis is based on histological examination of affected tissue sample. The treatment is conducted with antibiotic therapy, administering high doses of intravenous antibiotics and, in certain cases, surgical treatment, as was the case in our patient.
Keywords: *actinomycosis, postmenopausal bleeding, intrauterine contraceptive device*

RESULTS OF TREATMENT WITH MYO-INOSITOL AND D-CHIRO-INOSITOL COMBINATION IN RATIO 5:1 IN WOMEN WITH CLINICAL AND BIOCHEMICAL HYPERANDROGENEMIA ASSOCIATED WITH POLYCYSTIC OVARY SYNDROME

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Problem statement: Hyperandrogenemia is a part of the polycystic ovary syndrome (PCOS), which occurs in 5-15% of women of reproductive age. The most common complaints at a gynecologist`s appointment are menstrual disorders, hirsutism, acne and alopecia. The objective was to compare the effectiveness of the combination of myoinositol (MI) and D-chiro-inositol (DHI) in a ratio 5:1 and standard antiandrogenic therapy (COC containing ethinylestradiol 0,02 mg with drospirenone 3 mg) for the treatment of clinical and biochemical hyperandrogenemia, as well as to assess the degree of anxiety on the Spielberger-Khanin anxiety scale before and after therapy. ***Methods:*** Patients of the main group (N=53, aged 26.6±3.62) received an oral combination of 1000 mg MI and 200 mg DHI in a ratio of 5:1, 2 times a day after meals. Patients of the control group (N=55, aged 27.1±2.54) received COC for 6 months. The assessment of hirsutism on the Ferriman-Gallway (FG) scale, the severity of acne on the G. Plewig, M. Kligman scale were carried out initially and 2 months after the discontinuation of therapy. ***Results:*** There was a decrease in the levels of androgens in the serum blood in both groups. In the main group, the cancellation of therapy occurred in 1 patient due to nausea vs in 5 patients in the control group due to the occurrence of headaches (n=2), decreased libido (n=1), anomal uterus bleeding (n=2). A decrease in hirsutism on the FG scale was greater receiving COC (from 10.4±4.3 to 7.7±3.6, p=0.04) than inositols (from 10.1±3.9 to 8.9±3.7, p=0.076). After 6 months of therapy, there was a decrease in the severity of acne in both groups. However, in the first month after the withdrawal of COC, 35% of patients had an exacerbation of acne vs 10% in the main group. An improvement in the psychoemotional state of the patients due to a decrease in anxiety was more common in group 1 than in group 2. ***Conclusion:*** The results of the study showed that the combination of MI with DHI in a ratio 5:1

can be considered as an effective alternative therapy for the treatment of hyperandrogenemia in patients with PCOS.

ENDOMETRIOSIS HIDDEN BEHIND MENOPAUSE

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Problem statement: Endometriosis, believed to be an estrogen-dependent chronic inflammatory disease, classically affects women of reproductive age. The occurrence of de novo endometriosis diagnosis in postmenopausal women has recently suggested a shift in this paradigm. The pathophysiology and clinical management of this condition remain a challenge. The present study aims to contribute to a better understanding of endometriosis after menopause. ***Methods:*** A total of 367 patients with histologic evidence of endometriosis were included in this cross-sectional study. Pearson linear correlations with collected data and further qualitative synthesis statistics were performed using IBM® SPSS® v27. ***Results:*** The study sample included 9 cases (2.45% prevalence) of postmenopausal de novo endometriosis diagnosis. Mean age at endometriosis diagnosis was 60 years [50-85]. Mean time interval between endometriosis and menopause diagnosis was 6 years [1-28]. Mean BMI was 25.43 Kg/m2 [21.0-40.16]. One patient was under menopausal hormone therapy (MHT) with Low dose oral combined therapy. Two patients were symptomatic: one of them, who was under MHT, reported pelvic pain, and the other pelvic pain and dyspareunia. In the remaining asymptomatic patients, endometriosis was suspected from routine pelvic ultrasound findings of ovarian masses (n=3) and from surgical incidental findings during hysterectomy due to benign uterine disease (n=4). Ovarian localization prevalence was 77.78%. Nevertheless, a weak correlation was observed between CA-125 values and ovarian endometriosis localization (r=0.180, CI95% [-0.99;0.39]). All patients were submitted to surgical treatment: bilateral adnexectomy (n=4), total hysterectomy with bilateral adnexectomy (n=4) and cystectomy (n=1). No patient underwent hormone therapy after surgical treatment and none of them reported recurrence of symptoms or endometriotic lesions. One patient was diagnosed with clear-cell ovarian carcinoma at the same time of endometriosis diagnosis and was the one with the highest CA-125 values. ***Conclusion:*** This study highlights the lack of robust data related to endometriosis in postmenopausal women. Diagnosis of endometriosis and the risk of malignant transformation in menopausal women remain uncertain. Therefore, high-quality studies in this field are mandatory.

Disclosure of interest: *The authors declare that they have no conflict of interest.*

CERVICOVAGINAL AGENESIS DIAGNOSIS AND MANAGEMENT CHALLENGES ON A 14 YEARS OLD FEMALE FROM A REMOTE AREA: A CASE REPORT

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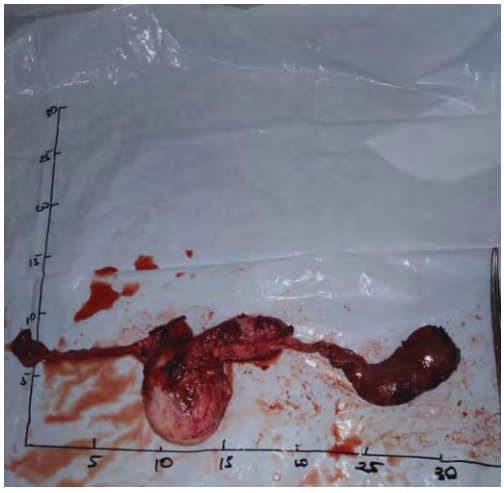
Problem statement: Cervicovaginal agenesis, accompanied by normal functional endometrium, is a rare but challenging Mullerian anomaly in the case of surgical treatment. Several studies report successful conservative surgical treatment, but the recommended treatment of cervicovaginal agenesis with a normal uterus was hysterectomy because of the high failure rate of uterovaginal anastomosis and also the risk of severe pelvic infection and sepsis. The objective of this case report is to highlight the challenge and experience in diagnosing and managing such a rare and dilemmatic case with limited settings based on patient difficulties in compliant to the regular follow-up visits and regular use of vaginal dilators after surgery due to adverse access to the hospital. ***Methods:*** This is a case report of a 14 years old para 0 who was first diagnosed with primary amenorrhea and imperforate hymen. Referred to the hospital from a remote area with cyclic abdominal pain and hematuria. Mobile abdominal mass was found and no sign of vagina canal or dimple and no hymenal fringe were found on physical examination. The abdominal computed tomography (CT-SCAN) featured a 53 mm hypodense homogen mass diameter inside the vesicouterine pouch pressing the uterus and base of the urinary bladder to right lateral, a 33.9 mm uterus diameter, small or thin vagina, and no appearance of left renal. The patient then diagnosed with vagina agenesis. Diagnostic laparoscopic found hematometra and hematosalphing. Open laparotomy discovered 20 cc foul smelling hemoperitoneum, round end and blind lumen of the lower uterine body lacked of uterosacral and cardinal ligament attachment with uterine sized 12 cm, both ovarium were intact, and no cervix was detected confirmed by histopathology examination as cervix agenesis. Hysterectomy was performed after counselling and informed consent had carefully done. ***Results:*** There were no complications following surgery. The patient and family acknowledged the permanent infertility and the chances to undergo reconstructive surgery when the patient reached adulthood. ***Conclusion:*** Cervicovaginal agenesis diagnosis and treatment is challenging due to rarity and variety of this case, while infertility is the main concern of this diagnosis. Every case must be reported to add publication literature as reference.



ASSOCIATION OF MMP-9 ACTIVITY ON THE INVASION PROCESS OF ENDOMETRIOMA TISSUE ON CHORIONIC ALLANTOIC MEMBRANE (CAM)

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Problem statement: Endometrioma occurs through a complex process. Various theories have been proposed, including the invagination of the ovarian cortex either secondary to bleeding of the superficial implant (Hugheson, 1957) or secondary to metaplasia of coelomic epithelium in cortical inclusion cyst (Donnez, 1996), and endometriotic transformation of a functional cyst (Nezhat, 1992). According to Hughesdon`s theory, endometrioma was originated from the accumulation of menstrual debris that

formed a pseudocyst and causing invagination of the ovarian cortex. Inflammation and fibrosis associated with endometrioma in cortical tissue enhanced follicular recruitment and atresia, resulting in focal exhaustion of primordial follicles responsible for reducing ovarian reserve. The implantation and invasion of endometrial tissue on the outer surface of the ovary is an essential initial process in the formation of endometrioma and is highly dependent on the proteolysis action of the matrix metalloproteinase. The previous study found an increased expression of MMP-9 in endometriosis. The association of MMP-9 on the ability of endometriosis to invade the cortex ovary remains unclear. This study aims to measure the correlation between MMP-9 and the capability of endometrioma tissue to invade the ovary by using the chorionic allantoic membrane (CAM) as a medium of tissue implantation. ***Methods:*** Ten samples of endometrioma tissue cultured in CAM, incubated for five days, then harvested for specimens. Samples were stained with hematoxylin-eosin, and the invasion scores were subsequently observed under a light microscope. The activity of MMP-9 was evaluated by using the gelatin zymographic method. Data were analyzed using the Spearman rank correlation test and Pearson correlation test. This research is still ongoing with a planned number of eighteen endometrioma tissues while only ten samples had been analyzed. ***Results:*** There was a strong significant positive correlation between MMP-9 activity and the invasion score of the endometrioma tissues. (r = 0.825; p= 0.03). Based on the ASRM score, the severity of endometriosis showed a weak positive correlation in the association with MMP-9 activity (r = 0.207; p= 0.565). ***Conclusion:*** There was a strong correlation between MMP-9 activity and invasion score of endometrioma, where the higher MMP-9 activity will increase the degree of endometrioma invasion.

OFFICE HYSTEROSCOPY AS A FEASIBLE METHOD FOR DIAGNOSING AND TREATING INTRAUTERINE LESIONS - DATA OF A PRIVATE OFFICE IN HUNGARY

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Problem statement: Minimally invasive procedures widespread and preferred all over the word in all field of medicine. In gynecology diagnosis and treatment of intrauterine lesions, hysteroscopy accepted as gold standard method. There is no need for anesthesia, operating theater with its high costs, therefore office hysteroscopy is more cost-effective compared to the traditional one. Out-patient hysteroscopy is even more preferred in pandemic times minimizing personal contacts and preventing complex surgeries in the operating theatre. ***Methods:*** Office hysteroscopy has been performed in private gynecological office. For diagnostic procedures a 2.9 mm optic is used with a 3.7 mm outer diameter sheath. For operative hysteroscopies a 5.5 mm sheath with working channel is used, that through scissors and grasper can be inserted to the uterine cavity. After 12 years, 6.5 mm diameter bipolar resectoscope has been introduced for operative surgeries. Besides infertility, bleeding disorders, or abnormal ultrasonographic result, lost IUD were the indications of the hysteroscopies. For resectoscopies nitrogen oxidul gas, paracervical blockage or local anesthesia could be offered. ***Results:*** Between 01.01.2020. and 14.09.2021. 361 hysteroscopies were performed. Surgery was successful in 355 cases. Main indications were primary infertility in 148 cases (age: 34.03±5.52), secondary infertility in 68 cases (age: 36.00±5.13), abnormal result of ultrasonography in 81 cases (age: 42.29±11.51) and abnormal uterine bleeding in 33 cases (age: 44.26±5.45). Diagnostic hysteroscopies were performed in 47 cases, as a part of infertility work-up in 49 cases tubal test was performed during hysteroscopy. We resected endometrial polyp in 42 cases mechanically and in 28 cases by resectoscope. Transcervical resection of myopia were performed in 13 cases, septum was resected in 8 cases and metro-pasty were performed in 8 cases to correct dysmorph uterus. Lost IUD was found in 5 cases and in 1 case it was repositioned. ***Conclusion:*** In several gynecological disorders office hysteroscopy gives the solution not only in diagnostics, but treatment, as well. Being an office procedure in effectivity, safety and expense point of view preferable over the traditional way.

REDUCTION IN MENSTRUAL BLOOD LOSS (MBL) IN WOMEN WITH UTERINE FIBROID (UF)-ASSOCIATED HEAVY MENSTRUAL BLEEDING (HMB) TREATED WITH RELUGOLIX COMBINATION THERAPY (REL-CT): LIBERTY LONG-TERM EXTENSION (LTE) STUDY

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Problem statement: In LIBERTY1&2 (24-week, double-blind, placebo-controlled studies), Rel-CT (relugolix 40mg, estradiol 1mg, norethindrone acetate 0.5mg) reduced MBL in women with UF-associated HMB. Effects of treatment on MBL volume in women receiving Rel-CT for up to 52 weeks, or in women who transitioned from placebo (after 24 weeks) to Rel-CT for up to 28 weeks, were assessed. ***Methods:*** Women who completed LIBERTY1&2 were eligible to enroll in a 28-week LTE study. All received Rel-CT. Primary efficacy endpoint: women (%) who achieved/maintained MBL 80 mL and ≥50% reduction from pivotal study baseline to the last 35 days of treatment. Secondary endpoints: mean MBL (%) reduction and amenorrhea rate. Outcomes were analyzed by baseline LIBERTY treatment assignment (Rel-CT/placebo) using descriptive statistics without statistical testing for treatment comparison. In LIBERTY1&2, study drug was initiated within 7 days of menses onset. In the LTE, the placebo group initiated Rel-CT later in the menstrual cycle because they had to complete Week 24 (W24) feminine product collection before transitioning. Data are reported for Rel-CT and placebo→Rel-CT groups for entire 52-week treatment period. ***Results:*** With Rel-CT (N=163), a rapid reduction in MBL was observed at W4 (least square [LS] mean % change from baseline: –52.8%), reaching –81.2% at W8 and maintained through W52 (–89.9%). With placebo (N=164), no meaningful MBL change occurred by W24 (–17.6%) nor did MBL decrease at time of the first bleeding after transition to Rel-CT because Rel-CT was initiated later in the menstrual cycle. At W32, MBL rapidly reduced (–79.6%), reaching –91.9% at W52, confirming the effect of Rel-CT shown in LIBERTY1&2. At W52, MBL 80 mL was observed in 87.1% and 75.6% and a ≥50% reduction of MBL was reported in 89.0% and 81.1% of women in the Rel-CT and placebo→Rel-CT groups, respectively. Women (%) achieving amenorrhea over the last 35 days of treatment: 70.6% (Rel-CT) and 57.9% (placebo→Rel-CT). ***Conclusion:*** Rel-CT resulted in rapid and clinically meaningful reduction of MBL in women with UF, which was maintained through W52. Treatment effect onset was faster when Rel-CT was initiated at the start of menses.

Study funded by Myovant Sciences GmbH.

MINIMALLY INVASIVE SURGERY APPROACH USING LIGASURE DEVICE FOR MANAGEMENT OF HERLYN-WERNER-WUNDERLICH SYNDROME: A CASE REPORT

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Problem statement: Herlyn-Werner-Wunderlich (HWW) syndrome is a very rare female congenital anomaly of urogenital tract involving Mullerian ducts and mesonephric duct. The triad characteristic of this syndrome includes didelphys uterus, obstructed hemivagina, and ipsilateral renal agenesis. The most common presentation is abdominal pain, dysmenorrhea, and abdominal mass secondary to hematocolpos. Often from ultrasound examination it can be suggested as cystic lesions or chocolate cyst. ***Method:*** this case, a 29 years old nulliparous woman, was referred to our hospital because of finding right kidney agenesis, and suspecting chocolate cyst in the ovary. Since menarche, patient complaining of dysmenorrhea that disturbed her daily activities with intermenstrual spotting. Now, she complaining there was a lump came out from vagina and disturbed her sexual activities. On physical examination, there was a lump in the right lateroanterior wall of vagina while straining, a longitudinal vagina septum was palpated, cervix couldn`t be visualized, uterus was difficult to assessed. Ultrasound revealed uterus didelphys with ground glass appearance right adnexal mass. Magnetic Resonance Imaging showed uterus didelphys, vaginal septum with right-sided hematocolpos, right kidney agenesis in accordance with feature of Herlyn-Werner-Wunderlich syndrome, bilateral functional ovarian cysts. Laparoscopy showing a complete duplication of the uterus from the horn to the cervix with no connection between the two uterine cavities, both ovaries, and left tube were normal, right tube was enlarged and salpingostomy was done using Ligasure device, right kidney was not visualized. The laparoscopy guiding diagnostic and operative management of the vaginal septum resection using Ligasure device was performed. ***Result:*** vaginal septectomy using Ligasure device give satisfying result and less bleeding. She was discharged 3 days after surgery and came for follow-up after 7 days. Vaginal examination revealed a healthy wound with no adhesion. ***Conclusion:*** HWW Syndrome is a rare condition. Some of the various syndrome types may go unnoticed for months or even years after the onset of menstruation. Early diagnosis, followed by proper surgical treatment, is the key to avoid potentially severe complications. Our case introduces an innovative and safe alternative to the surgical management of a longitudinal vaginal septum, particularly useful in a confined surgical space.

THE EXPRESSION OF TUMOR NECROSIS FACTOR-ALPHA IN ENDOMETRIOMA AND BENIGN CYST

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Problem statement: Expression of tumor necrosis factor-alpha (TNF-A) as one of the pro-inflammatory cytokines has been suggested as a specific event for the maintenance and progression of endometriosis. In women with endometriosis, TNF-A concentrations correlate with the stage of the disease. Ovarian endometrioma is a common phenotype of endometriosis. The development of endometrioma may be correlated with the expression of TNF-A, but there is still a lack of research on TNF-A in endometrioma. The aim of this study was to investigate the expression of TNF-A in women with endometriomas compared with the benign cyst. ***Methods:*** In total, 46 patients undergoing surgery for ovarian cysts were evaluated, and a diagnosis of benign cyst or endometriomas was determined. Expression of TNF-A was evaluated in endometriomas from 24 women and 22 women with benign cysts were determined by performing immunohistochemical. ***Result:*** In this study, the mean age in years for the endometrioma group was 35.54 and 36.86 in the benign cyst group. In the benign cyst group, the majority were cases of serous cystadenomas (n=9), mature teratoma (n=5), and functional cyst (n=7). The degrees of endometriosis in this study included severe degrees (66.7%), moderate degrees (16.7%), and mild degrees (16.7%). The mean difference between the two groups was found. The Expressions of TNF-A were higher in endometriomas than in benign cysts with p 0.05 indicating a statistically significant difference, but this study also found that the increased expression of TNF-A did not correlate with the degree of endometriosis (r= 0.666 ; p0.05). ***Conclusion:*** For TNF-A, the immunohistochemical staining was qualitatively more intense in endometriomas, furthermore, the expression was different significantly, but this study also found that the increased expression of TNF-A did not correlate with the degree of endometriosis. These results indicate that the analysis of TNF-A should be further evaluated as a tissue marker for endometriomas.

HPV

AWARENESS OF HUMAN PAPILLOMAVIRUS VACCINATION AMONG WOMEN IN KAZAKHSTAN

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Problem statement: For Kazakhstani women, human papillomavirus (HPV) remains one of the major health threats. However, many women remain unaware of HPV vaccination. The aim of this study was to determine the awareness of HPV vaccination and to identify the differences in HPV vaccine awareness among women from between different the regions in Kazakhstan. ***Methods:*** Paper-based questionnaires were collected from 1,215 women in the age group of 18-70 years old during their visits to gynecologists at the cities in five Kazakhstan regions (Nur-Sultan - capital city, Almaty - southern, Aktobe - western, Oskemen - eastern, and Pavlodar - northern region). A multivariable logistic regression model was constructed for data analysis. ***Results:*** In total 1,215 women participated in the study. Half of the respondents (51%) were aware of the HPV vaccine. The mean age was 36.51±10.03, and the majority (38%) were aged between 26 and 35. Most of the women (70%) identified themselves ethnically as Kazakh. Half of the respondents (53%) have university degrees. The majority of women (80%) were either married or had a partner. In comparison with the women in the age group of 18-25 years old, women aged older than 46 were 2.27 times more likely to be aware of HPV vaccination. In contrast to women from the capital city, women from the northern region were more likely to be aware of HPV vaccination. The respondents in committed relationships were 1.65 times more likely to be aware of HPV vaccination. Women with a high level of knowledge about cervical cancer and HPV were more likely to be aware of HPV vaccination in comparison with the participants who have a low level of knowledge, 1.66 and 1.23-fold respectively. ***Conclusion:*** This study revealed that 51% of women who visited gynecologists in

Kazakhstan were aware of HPV vaccination. However, in order to contribute to health policy formation and decision-making about HPV vaccination and cervical cancer prevention, there is also a need to study more about vaccine acceptance among the Kazakhstani population.
Disclosure of interest: *This study was supported by the Nazarbayev University Grant Number is 110119FD4528, 2019-2021.*

ADENOCARCINOMA OF CERVIX – A DIAGNOSTIC CHALLENGE

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Problem statement: Cervical cancer is the sixth most commonly diagnosed cancer in Europe1and the third leading cause of cancer death among females in less developed countries, which contains 90% of cervical cancer deaths. Huge differences are explained by the availabling of screening and prevalence of human papillomavirus (HPV). 2Screening with HPV testing and adequate treatment of percursors of cervical cancer had changed the paradigma of this disease. Squamous cell carcinomas (SCC) represent nearly 75% of all cervical cancer and adenocarcinoma 15%, leading to the majority of follow-up studies being of SCC cases. Although, some risk factors are shared with SCC, particularly infection with high-risk subtypes of HPV (specially type 16 and 18), factors such as cigarette smoking do not appear to be a risk factor for adenocarcinoma. ***Methods:*** Description of a clinical case ***Results:*** 56 years old woman with past history of premature ovarian failure at 39 years old, presents with a HPV 16 and 33 positive with a normal citology. One year later, citology showed a HSIL with HPV persistency. At colposcopy, a biopsy was performed that revealed a CIN2. An excisional treatment with electrosurgical conization was decided and anatomopatological result was: CIN1 and a focus of 1mm of CIN2, margins free of lesion. At 6 months, a transformation zone tipo 2 was observed with findings suggestive of a low-grade lesion and a biopsy was performed at 1 and 8 o'clock. On citology, LSIL and adenocarcinoma on glandular cells at endocervical component and HPV testing was positive for type 16 and other of high risk. Re-conization was proposed to the patient. ***Conclusion:*** Adenocarcinoma represents a minority of cervical cancer and includes a more heterogeneous group. This clinical case demonstrates the clinical importance of post-treatment surveillance, in fact, although HPV testing is described as the best option to follow-up treated patients, in some cases, citology has a very important role.

OTHER

DIAGNOSIS AND APPROACH TO INTERSTITIAL ECTOPIC PREGNANCY: PURPOSE OF A CASE

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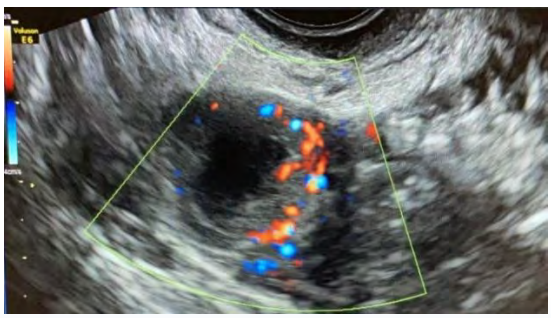
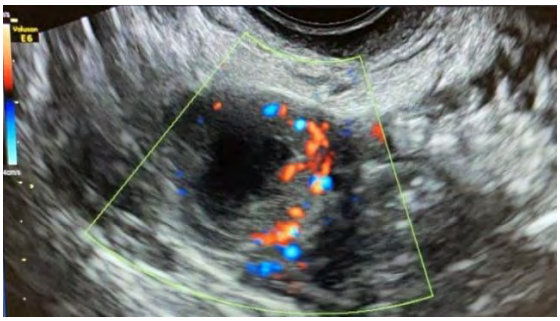


Ectopic pregnancy occurs in 2% of all pregnancies and of these, 95% are in the fallopian tubes, however, there are very rare locations that are called non-tubal ectopic pregnancies as they are, for example, at the interstitial level. Interstitial ectopic pregnancy represents up to 4.2% of ectopic pregnancies. Risk factors for this presentation include a previous ectopic history, uterine abnormalities, and the use of assisted reproductive techniques. 38-year-old G2E2 female patient with a history of 4 in vitro procedures, who was referred for outpatient consultation due to non-progression of BHCG and an extra-institutional transvaginal ultrasound finding of a left adnexal ectopic pregnancy. An institutional transvaginal (TV) ultrasound was performed showing a left lateral fundic interstitial ectopic pregnancy with a live embryo, with 5 weeks and 6 days gestation. A TV ultrasound guided laparoscopic puncture of the gestational sac with potassium chloride and methotrexate saccular injection was considered. However, due to satisfied parity and low probability of pregnancy due to a history of vasectomy by the partner, they chose to perform a hysterectomy with bilateral salpingectomy. The hysterectomy was performed, finding a left interstitial ectopic pregnancy of approximately 3 cm. The management of interstitial ectopic pregnancy has different points of view which must be taken into account. Types of management include intramuscular injection of methotrexate, intra-amniotic potassium chloride, hysteroscopy, laparoscopy, expectant management, or hysterectomy.



In asymptomatic patients or with mild symptoms, the use of methotrexate is preferred, and local injection is the most recommended due to its safety and greater efficacy, rather than systemic or surgical management. Similarly, in the case presented there was the presence of fetocardia, for which, local injection or surgical management is preferred, since systemic management can present up to 30% of therapeutic failure. Finally, although surgical management is indicated mainly in cases of uterine rupture or in hypovolemic shock, in this case it was important to take into account the satisfied parity of the patient, the low probability of spontaneous pregnancy due to medical history, and not least, the location of the ectopic pregnancy, which has a high risk of complications, including heavy maternal bleeding.

SURGICAL MANAGEMENT OF CERVICAL ECTOPIC PREGNANCY AFTER SYSTEMIC METHOTREXATE: A CASE REPORT

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Problem statement: Cervical ectopic pregnancy is a rare condition with an incidence of less than 1% of all ectopic pregnancies. It is associated with high mortality and morbidity due to life threatening severe haemorrhage. Management options include medical management and surgical procedures, all with the goal of fertility preservation. We describe a case managed with medical therapy that went on to require surgical intervention. ***Methods:*** A 26-

year-old nulliparous female presented to the emergency department of a rural hospital with vaginal bleeding after six weeks of amenorrhoea. She had type 2 diabetes mellitus on liraglutide, with no other medical or surgical history. This was an unplanned pregnancy. The β-subunit of human chorionic gonadotropin (βhCG) titre was 32 924. Based on transvaginal ultrasound, a live endocervical gestation was identified with a crown rump length measuring 9.8mm, equivalent to 6+5 weeks gestation. A diagnosis of a live endocervical ectopic pregnancy was made. ***Results:*** The patient received systemic multi-dose Methotrexate therapy via intramuscular injection 50mg/m² for four doses, with ongoing outpatient monitoring. 16 days later, she presented to a different rural emergency department with abdominal pain and bleeding. The βhCG was now 6381 and there was a persistent cervical gestational sac on transvaginal ultrasound. Due to ongoing bleeding requiring blood transfusion, the decision was made to perform a suction curettage under general anaesthesia. The patient underwent bilateral ligation of the cervicovaginal branches of the uterine arteries, suction evacuation of retained pregnancy products, uterine curettage, and placement of a Foley catheter in the cervix kept in place by a McDonald's cervical cerclage. The uterine arteries were pre-operatively catheterised but embolization was not required. The Foley catheter and cerclage were removed two days later. She required a total of four units of blood during the admission and the βhCG level fell to zero after 45 days. There were no further reported complications. ***Conclusion:*** Given the rarity of the condition, it is difficult to establish evidence-based criteria for management of cervical ectopic pregnancy. The early diagnosis and prompt treatment were crucial in this case for fertility preservation in this patient.

Disclosure of interest: *None.*

EUTHOPIC OR ECTOPIC PREGNANCY: THAT IS THE QUESTION

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Problem statement: Congenital uterine anomalies (CUA) are result from abnormal formation, differentiation, and fusion of the Müllerian or paramesonephric ducts during fetal life. Itsprevalence is reported to be 4.3-6.7% in the general population and 12.6-18.2% in those with recurrent miscarriages. Several classifications have been proposed in order to categorize CUA, though the European Society of Human Reproduction (ESHRE) classification seems to be the most accepted. Actually, this classification is used by clinicians when they refer to CUA to evaluate not only their clinical impact, but also pregnancy outcomes. We report a case of pregnancy in a rudimentary uterine cavity which was misdiagnosed as an ovarian ectopic pregnancy. ***Methods:*** A 38-year-old woman, G2P1 with previous lower segment cesarean (breech presentation) and no relevant gynecological history, was admitted to emergency department (ED) with moderate vaginal bleeding and pelvic pain, with hemodynamic stability. On transvaginal ultrasound examination, we found an anteversion uterine cavity with endometrial thickness of 16 mm and an evolutive pregnancy compatible with 8 weeks, placed outside the uterine cavity. There was a suspicion of right ovarian ectopic pregnancy (normal ovarian stroma surrounding the gestational sac). In this context, a diagnostic laparoscopy was performed. ***Results:*** Intraoperatively, two similar size uteri were observed: on the left side, a main uterus with hard consistency and no macroscopic changes, and on the right, there was an enlarged and soft pregnant uterus with no rupture. Both of them had a correspondent adnexa (right to the pregnant cavity and left to the main cavity). In addition, we also noticed the presence of a communication between both uteri. After the identification of anatomical structures, right hemi-hysterectomy with bilateral salpingectomy was done. The anatomopathological exam reported a rudimentary uterine cavity with endometrial changes related to pregnancy and an embryo. ***Conclusion:*** We have reported a case of ACU class U4a, based on of ESHRE classification, that comprises an hemiuterus with a functional rudimentary horn. In this rare case, the accurate identification and treatment of this entity is crucial to avoid complications such uterine rupture and its severe outcomes. Therefore, this case report emphasizes the importance of recognizing and managing properly the ACU.

EFFECTS OF AN ORAL CONTRACEPTIVE CONTAINING ESTETROL AND DROSPIRENONE ON SELECT ENDOCRINE, METABOLIC AND HEMOSTATIC PARAMETERS: RESULTS OF A PHASE-2 TRIAL

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Problem statement*:* To evaluate the effect of a new combined oral contraceptive containing the native estrogen Estetrol (E4) 15 mg and drospirenone (DRSP) 3 mg on endocrine, metabolic, and hemostatic parameters. ***Methods****:* We conducted a single-center, randomized, open-label, three-arm, parallel study in healthy women. Participants received six consecutive treatment cycles with E4/DRSP (n=38), or ethinyl estradiol (EE)-containing reference products, EE 30 µg/levonorgestrel (LNG) 150 µg (n=29) or EE 20 µg/DRSP 3 mg (n=31). We compared median percentage changes between baseline and cycle 6 for all parameters. ***Results****:* E4/DRSP had smaller effects than EE/LNG and EE/DRSP on angiotensinogen (+75.0% versus +170.0% and +206.5%, respectively), sex hormone binding globulin (+55.0% versus +74.0% and +251.0%, respectively), cortisol (+26.0% versus +109.0% and +107.0%, respectively), cortisol binding globulin (+40.0% versus +152.0% and +140.0%, respectively), and thyroxin binding globulin (+17.0% versus +37.0% and +70.0%, respectively). E4/DRSP minimally changed lipid parameters, with the largest effect on triglycerides (+24.0%), a change similar to EE/LNG (+28.0%) and less than EE/DRSP (+65.5%). E4/DRSP had less pronounced effects than EE/LNG and EE/DRSP on endogenous thrombin potential-based activated protein C resistance (+30.0% versus +164.5% and +218.5%, respectively) and prothrombin fragment 1+2 (+23.0% versus +71.0% and +64.0%, respectively), two procoagulant markers. E4/DRSP also had less impact on plasminogen (+12.0% versus +40.0% and +35.5%, respectively) and tissue plasminogen activator (-7.0% versus -33.0% and -39.5%, respectively), two fibrinolytic proteins. ***Conclusions****:* E4/DRSP has a limited effect on endocrine and metabolic parameters and a neutral hemostatic profile compared to EE-containing products.

This study was funded by Estetra SRL, an affiliate company of Mithra Pharmaceuticals. CK and ID are directors of Dinox BV. JD is the director and founder of Qualiblood. Both companies are CROs that received funding from Mithra. MJ is an employee of Estetra SRL. MDC serves on an Advisory Board for Evofem, Mayne, Merck and Searchlight and is a consultant for Danco, Estetra SRL, Mayne, Medicines360 and Merck. The university of California, Davis, receives contraceptive research funding from Dare, HRA Pharma, Medicines360, Merck and Sebela. JMF is a member of the board at Mithra Pharmaceuticals and received financial support for the supervision of this study.

BLEEDING PATTERNS WITH USE OF AN ORAL CONTRACEPTIVE CONTAINING ESTETROL AND DROSPIRENONE: POOLED ANALYSIS OF PHASE-3 CLINICAL TRIALS

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***Problem statement**:* To evaluate bleeding patterns with use of a 24/4-day novel combined oral contraceptive regimen containing estetrol, a native estrogen, and drospirenone. ***Methods**:* We pooled bleeding data from two parallel, multicenter, open-label, phase-3 trials (United States/Canada and Europe/Russia). Healthy women aged 16-50 years with body mass index of 18-35 kg/m2 used estetrol 15 mg/drospirenone 3 mg for up to 13 cycles. Participants reported vaginal bleeding (blood loss requiring use of sanitary protection) or spotting (minimal blood loss, requiring no new use of sanitary protection) on daily diaries. We evaluated bleeding outcomes in participants that started treatment and had at least one evaluable cycle. We calculated mean frequency of scheduled and unscheduled bleeding and/or spotting and median duration of bleeding and/or spotting episodes. ***Results**:* Of 3,417 participants starting treatment, 3,265 were included in the bleeding analysis. Mean reported treatment compliance was ≥99%. Across cycles, 87.2-90.4% of participants reported scheduled bleeding/spotting, with a median duration of 4-5 days/cycle. Unscheduled bleeding/spotting frequency decreased from 27.1% in Cycle 1 to 17.5% from Cycle 5 onwards, with a median duration of 3-4 days/cycle and most episodes (62.7%) were spotting-only. Of 2,234 women completing 13 cycles, 754 (34%) reported unscheduled bleeding/spotting in only 1 or 2 cycles and 911 (41%) did not report any unscheduled bleeding/spotting. The most common bleeding adverse events (AEs) considered treatment-related were 'metrorrhagia' (159 [4.7%]) and 'vaginal hemorrhage' (101 [3.0%]). One-hundred and four (3.0%) participants discontinued for a bleeding-related AE. ***Conclusion**:* Most users of estetrol/drospirenone oral contraceptive experience a predictable bleeding pattern and limited unscheduled bleeding.

This study was funded by Estetra. AMK serves on Advisory Board for Merck and Mithra. University of Florida receives funding from Merck and Estetra. SLA received consulting fees from Mayne and Merck. Magee-Womens Research Institute receives research funding from Estetra, EvoFem, Merck. MJ is an employee of Estetra. JMF is board member at Mithra and received financial support for supervision of this study. MDC serves on Advisory Board for Evofem, Mayne, Merck, Searchlight and is consultant for Danco, Estetra, Mayne, Medicines360, Merck. University of California, Davis, receives funding from Dare, HRA Pharma, Medicines360, Merck, Sebela.

POOLED PHASE-3 ANALYSIS OF EFFICACY AND SAFETY OF ESTETROL/DROSPIRENONE COMBINED ORAL CONTRACEPTIVE

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***Problem statement**:* To examine efficacy and safety of a combined oral contraceptive containing the native estrogen estetrol (E4) and drospirenone (DRSP) in a 24/4-day oral regimen. ***Methods**:* Two parallel, multicenter, open-label, phase-3 trials (United States/Canada and Europe/Russia) enrolled healthy women 16-50 years to use estetrol 15 mg/drospirenone 3 mg (E4/DRSP) for up to 13 cycles. We pooled data in participants 16-35 years at screening to assess the Pearl Index (PI) in at-risk cycles (confirmed intercourse and no other contraceptive use). We also stratified PI by previous hormonal contraceptive use and body mass index (BMI) and compared groups using Chi-square testing. We evaluated overall safety (treatment-related adverse events [AEs]) in all participants aged 16-50 years. ***Results**:* We treated 3,417 participants with E4/DRSP of whom 3,027 were 16-35 years. Overall, participants reported ≥99% treatment compliance. Among women 16-35 years, PI was 1.52 (95% CI 1.04-2.16). For starters (n=1,368) and switchers (n=1,469), PI was 1.88 (95% CI 1.09-3.00) and 1.24 (95% CI 0.68-2.08), respectively (p=0.25). For BMI 25.0 kg/m2 (n=1,771), 25-30 kg/m2 (n=656) and ≥30 kg/m2 (n=410), PIs were 1.14 (95% CI 0.64-1.88), 2.19 (95% CI 1.05-4.03) and 2.27 (95% CI 0.83-4.94), respectively (p=0.17). The most frequently reported treatment-related AEs were metrorrhagia (4.7%), acne (3.3%) and headache (3.2%). Three treatment-related AEs (0.1%) were considered serious: worsening depression (continued treatment), ectopic pregnancy (discontinued) and venous thromboembolism (discontinued). ***Conclusion**:* Overall, and in subgroups stratified by contraceptive history and BMI, women using E4/DRSP demonstrated contraceptive efficacy. Adverse events occurred at low rates in the entire population.

JTJ received payments for consulting from Abbvie, Cooper Surgical, Bayer Healthcare, Evofem, Mayne Pharma, Merck, Sebela, Therapeutics MD. AMK serves on Advisory Board for Merck and Mithra Pharmaceuticals. The University of Florida receives funding from Merck and Estetra SRL. MJ is an employee of Estetra SRL. JMF is board member at Mithra Pharmaceuticals and received financial support for supervision of this study. MDC serves on Advisory Board for Evofem, Mayne, Merck and Searchlight and is consultant for Danco, Estetra SRL, Mayne, Medicines360 and Merck. The university of California, Davis, receives contraceptive research funding from Dare, HRA Pharma, Medicines360, Merck, Sebela.

ISOLATED CONGENITAL HYPOPLASIA OF NASAL CARTILAGE – A PRE NATAL ULTRASOUND DIAGNOSIS

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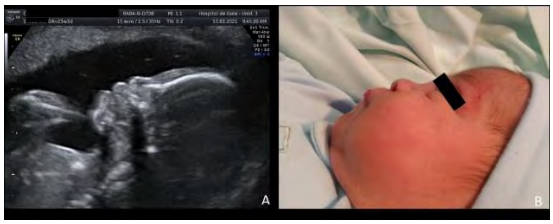
Problem statement: Prevalence of congenital nasal anomalies is about 1 in 20,000 to 1 in 40,000 live births. Fetal nasal bone anomaly, such as hypoplasia of the nasal bone, can be used as an ultrasound soft marker for screening of fetal chromosomal abnormalities, particularly trisomy 21 syndrome. It is also associated with some chromossomal microdeletions or microduplications which might be detected using microarray technology, thus improving detection rates for fetal conditions. Isolated non-syndromic congenital nasal anomalies are rare. Nasal bone hypoplasia can be present is 0.5-1.2% of normal fetuses on a routine 2nd trimester scan. ***Methods & Results:*** We report a 39-year-old pregnant woman, primigravida, with no previous gynecological surveillance, spontaneous pregnancy. She had history of lower limb deep vein thrombosis and hyperparathyroidism secondary to a parathyroid adenoma. First trimester ultrasound and combined screening for aneuploidies were considered low risk. At 20 weeks gestation, her second trimester scan

revealed an abnormal profile with a hypoplastic nasal bone measuring 4.7mm and a flat nose with a wide base (Figure 1- A). No other sonographic abnormalities were identified. Following parental counselling, amniocentesis was performed, for QF-PCR and subsequently microarray, which revealed normal results. Screening for infectious disease in blood was negative. Fetal echocardiogram was normal. Several subsequent growth scans were performed and she proceed her pregnancy uneventfully. A vaginal delivery occurred at 40 weeks of gestation. A healthy boy was born weighing 3800 grams and an Apgar score 9/10. Isolated hypoplasia of nasal cartilage was confirmed after birth (Figure 1–B). ***Conclusion:*** Prenatal diagnosis of facial dysmorphisms can be difficult. Many conditions presenting with low flat nasal bones have been described, although most of them were associated with other anomalies and genetic conditions. A careful evaluation of fetal anatomy should be undertaken, especially skeletal and heart assessment. Genetic and antenatal counselling must be offered to the parents.



INTERTWIN MEMBRANE VELAMENTOUS UMBILICAL CORD INSERTION IN A BICHORIONIC TWIN PREGNANCY

Mariana Lira Morais[1], Diana Monteiro[3], Marta Campos[2], Mariana Doria[3], Jorge Castro[2], Catia Lourenco[2], Monica Melo[2], Ana Olivia Sousa[2], Matilde Azevedo[2], Conceicao Brito[2]

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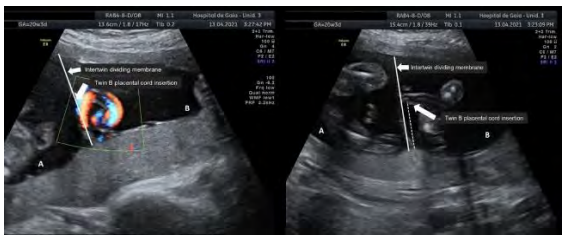
[3]*Obstetrics, Unidade Local de Saúde de Matosinhos, Matosinhos, Portugal*

Problem statement: Velamentous cord insertion (VCI) is defined as an abnormal insertion of the umbilical vessels into the fetal membranes before entering the placenta. The incidence of VCI ranges from 0.1% to 1.8% among all pregnancies and the risk is up to 10 times higher in multiple pregnancies, especially monochorionic twins. Some studies have reported that VCI is associated with an increased risk of adverse perinatal outcomes such as prelabor rupture of membranes (PROM), preterm PROM (pPROM), intrauterine growth restriction, low Apgar scores, placental abruption, vasa previa, placenta accreta spectrum and fetal and neonatal death. ***Methods & Results:*** We report a 30-year-old pregnant woman, primigravida, complicated by gestational diabetes. She had a total thyroidectomy for a papillary carcinoma of the thyroid in 2008, currently medicated with levothyroxine. First trimester scan was normal and revealed a bichorionic biamniotic twin pregnancy. First trimester combined screening for aneuploidies scored low risk. Her second trimester scan, at 20 weeks of gestation, revealed a velamentous cord insertion into the intertwin membrane (Figure 1) of fetus B. Both twins had normal morphology and posterior placenta. Since then, the ultrasound was repeated every 2 weeks to assess fetal growth. At 29 weeks' gestation, this gravida was hospitalized due to pPROM and preterm labor. She was given corticosteroids for lung maturation, magnesium sulfate for neuroprotection and antibiotic prophylaxis according to local protocols. She was delivered by an uneventful c-section because of breech presentation of both twins (twin A 1135 g, Apgar Index 6/7/8; twin B 1250 g, Apgar Index 8/9/9). The unusual velamentous placental cord insertion was observed after delivery and confirmed by pathological analysis. ***Conclusion:*** VCI is an important indicator of adverse perinatal outcome. As described in our clinical case, pregnancies with anomalous cord insertion appear to have increased risk of spontaneous preterm birth, PROM and pPROM. This finding suggests that the altered development of the placenta, cord and membranes may have a common etiology. Therefore, the identification of ultrasound predictors of adverse outcome (such as VCI) may be useful in risk stratification and management of twin pregnancies.



CONTRACEPTION USE AMONG WOMEN DIAGNOSED WITH MULTIPLE SCLEROSIS IN WESTERN UKRAINE

Oksana Nehrych[1], Vira Pyrohova, Vira Pyrohova[1], Tetyana Nehrych, Tetyana Nehrych[2], Nazar Negrych, Nazar Negrych[2]

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Problem statement: Multiple sclerosis (MS) is a leading cause of disability in young patients worldwide. MS-related problems significantly affect family planning, as the symptoms of the underlying disease may interfere with the full care of the child, and there are concerns about the possible inheritance of MS by future generations. The study aimed to evaluate awareness about contraception and usage of these methods about reproductive-aged women in Western Ukraine. ***Methods:*** A survey of 116 women of reproductive age with a confirmed diagnosis of multiple sclerosis, analyzed the use of various contraceptive methods and awareness of family planning. ***Results:*** Evaluation of patients` use of means of preventing unwanted pregnancies at the time of inclusion in the study showed an insufficient level of use of reliable contraceptives. The use of family planning methods was relevant for all women in the main cohort, except for those who did not have sex - 14 (12.1%) women. However, 69.8% of women had never consulted a specialist on effective family planning methods, only 17.2% of women after being diagnosed with MS were recommended to use contraception. Although interrupted intercourse is not a method of contraception, 41.4% of patients of early reproductive age and 18.8% of late reproductive age used it to prevent unplanned pregnancy. ***Conclusion:*** The critically low use of reliable, effective and safe contraceptives among women with MS increases the risk of adverse effects, including the birth of a sick child or abortion rates. Effective counseling on family planning is obligatoty for all women with MS, especially those taking disease-modifying drugs. Most methods of contraception are available for women with MS. When choosing the appropriate method, factors to consider include safety, availability, acceptability and effectiveness.

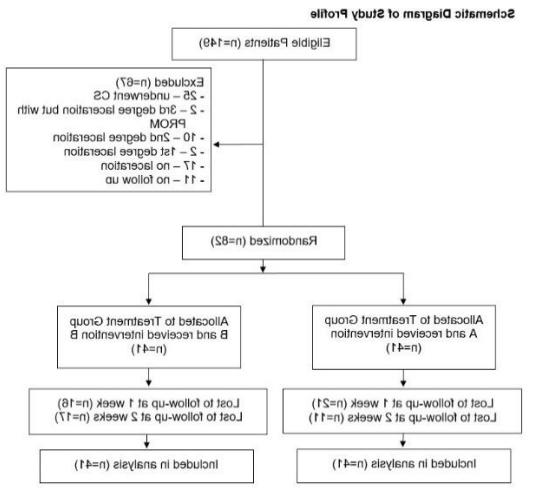
COMPARATIVE STUDY ON THE USE OF SINGLE-DOSE ANTIBIOTIC PROPHYLAXIS AND 7-DAY ANTIBIOTIC REGIMEN IN THE MANAGEMENT OF HIGH-ORDER PERINEAL LACERATION AFTER VAGINAL DELIVERY (A RANDOMIZED CONTROLLED TRIAL)

Almaira Pagayao[1], Josefa Dawn Martin[1]

Department of Obstetrics and Gynecology, Southern Philippines Medical Center, Davao City, Philippines

Background: Vaginal delivery is commonly associated with perineal lacerations that may increase infectious morbidity. Although prophylactic antibiotics reduce infection, unnecessary prolonged antibiotic use has associated risks. Single-dose antibiotic prophylaxis is recommended based on a single randomized controlled trial with low to moderate quality of evidence. ***Objective:*** This study was conducted to determine whether single-dose prophylaxis compared with a 7-day antibiotic regimen for high-order perineal lacerations will prevent wound complications. ***Methodology:*** This prospective randomized controlled study was approved by the Ethics Review Committee. Eighty two (82) pregnant women were included. Group A received single-dose Cefoxitin and Group B received 7-day regimen of Cefuroxime+/-Metronidazole. Pelvic exam was done at 24-48 hours, 1 week, and 2 weeks after delivery to monitor for wound complication. ***Results:*** Baseline profiles of both groups were comparable. At 24-48 hours postpartum, there was no significant difference in wound complications between the two groups (0% vs 7%,p=0.058). Intention-to-treat analysis at 1 week postpartum showed significantly more complications in Group B (0% vs 10%, P=0.020). At 2 weeks postpartum, none had wound complications in both groups. Birth weight 3kg, episiotomy, nulliparity and perineal length 3kg significantly increased the risk of wound complication (p=0.011). ***Conclusion:*** Single-dose Cefoxitin given at the time of repair of high-order perineal lacerations is more effective than 7-day regimen of Cefuroxime and Metronidazole in preventing wound complication at 1 week postpartum. No significant difference on incidence of wound complication was noted between the treatment groups at 24-48 hours and 2 weeks postpartum.

***Keywords*:** antibiotic prophylaxis, high order perineal laceration



RISK OF PREMATURITY IN IMMIGRANT MOTHERS WITH AND WITHOUT COMORBIDITIES: A POPULATION-BASED STUDY

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[2]*Research Center in Epidemiology, Biostatistics and Clinical Research (School of Public Health), Université Libre De Bruxelles (ULB), Brussels, Belgium*

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Problem statement: There is a known association between the immigration status of the mother and pregnancy outcomes, but its influence may vary according to the mother's comorbidities. Our objective is to evaluate how mother's comorbidities affect the relationship between maternal nationality and prematurity. ***Methods:*** This is a population-based study using the data from linked birth and death certificates from the Belgian civil registration system. Data are related to all singleton births to mothers living in Belgium between 2010 and 2016 (n=865,545). Maternal comorbidities were body mass index (BMI)30sqmt, hypertension (HT) and diabetes. Maternal nationality was defined as the nationality of the mother at her child`s birth, nationality groups were: Belgian, EU27, Easter Europe and Russia (noEU27),Turkey, North Africa and sub Saharan Africa. We used logistic regression to estimate the odds ratio for the associations between nationality and perinatal outcomes before and after adjusting for maternal comorbidities. We stratified for HTA and BMI. ***Results:*** Among women without HTA, prematurity rates are lower for non-Belgian women (all nationality groups) than Belgian women.OR adjusted by BMI and diabetes were: EU27 0.87(0.84-0.90), Easter Europe and Russia (noEU27) 0.81(0.74-0.88),Turkey 0.81(0.73-0.90), North Africa 0.58(0.55-0.62) and sub Saharan Africa 0.82(0.77-0.88) . In women with HTA the aOR for prematurity were: EU27 1.14(1.02-1.27), Easter Europe and Russia (noEU27) 1.25(0.95-1.64),Turkey 1.34(0.94-1.93), North Africa 1.33(0.94-1.93) and sub Saharan Africa 1.77(1.56-2.00). In women with a BMI 30Kg/sqmt Prematurity rates are lower for non-Belgian women (all nationality groups) than Belgian women, OR adjusted by HTA and diabetes were EU27 0.87(0.84-0.91), Easter Europe and Russia (noEU27) 0.83(0.76-0.9),Turkey 0.81(0.72-0.9), North Africa 0.6(0.56-0.64) and sub Saharan Africa 0.91(0.85-0.97). In women with a BMI 30Kg/sqmt, the aOR for prematurity were: EU27 1.01(0.92-1.12), Easter Europe and Russia (noEU27) 0.89(0.68-1.17),Turkey 1.18(0.89-1.55), North Africa 0.78(0.67-0.91) and sub Saharan Africa 1.14(1.01-1.30) ***Conclusions:*** Although immigrant women appear to have a lower risk of prematurity than Belgian women, in the presence of comorbidities (HTA or BMI 30kg/sqmt), their risk may be greater or equal to than Belgian women with the same comorbidities.

SALPINGITIS ISTHMICA NODOSA- A CAUSE FOR RECURRENT ECTOPIC PREGNANCY

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Obstetrics and Gynaecology, Stepping Hill Hospital, Stockport, UK

Problem statement: Salpingtis isthmica nodosa (SIN) is a condition which occours very rarely and is detected after histopathology of the tube and would require further assessment in a fertility set up to prevent any further possiblity of ectopic pregnancy from happening and hence appropriate counselling and further management. ***Methods:*** Salpinigitis isthmica nodosa is a condition that occours 0.6-11% prengancies , it is also called the diverticulosis of the fallopian tubes(1). In our early pregnancy unit we assessed a 28 year old lady who has one left sided ectopic pregnancy followed by a right sided ectopic pregnancy medically managed, had a normal vaginal dleivery and now come in pregnant 6 weeks with a left sided ectopic pregnancy, medical management of the ectopic pregnancy with methotrexate failed and hence was decided upon for surgical management with salpingectomy. ***Results:*** Left tube was sent for histopathology and it showed SIN. Patient was referred to the fertility unit for further management. ***Conclusion:*** There very few case reports and a literature regarding SIN and its etiology largely remains unknown, patients who have been diagnosed with SIN need to be appropriately managed to prevent further recurrence of ectopic pregnancies and morbidities from the same.

Disclosure of interests: *I have no conflicts of interests to this paper.*

Reference: *1. Majumdar B, Henderson PH, Semple E. Salpingitis isthmica nodosa: a high- risk factor for tubal pregnancy. Obstet Gynaecol. 2983 Jul; 62(1):73-8.*

PREGNANCY IN WOMAN WITH FOWLER SYNDROME

Shefali Rathee[1], Alina Vais[1]
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A favourable outcome of a 31 -year- old pregnant woman with underlying Fowler's syndrome along with focal epilepsy, Hypothyroidism and Asthma. Fowler's syndrome is a cause of urinary retention in young women. The abnormality lies in the failure of urethral sphincter to relax, hence the main concern is to ensure adequate bladder emptying. Our patient went through self- catheterisation and suprapubic catheters after which she had the Mitrofanoff procedure to help manage her symptoms. Upon getting pregnant the main concern was recurrent urinary tract infections and pelvic pain requiring hospital admissions for parenteral antibiotics and analgesia. She underwent Induction of labour at 39 weeks and delivered a healthy infant. Post- natal recovery was complicated with worsening of seizures, was managed with support of neurology team input.

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COGI Laser Course

December 2nd 2021
14.00 – 16.45, Hall B
Berlin, Germany

The 29th World Congress on Controversies
in Obstetrics, Gynecology & Infertility

Vaginal Erbium Laser for Women's Health

Course Program (165 minutes):

0. Introduction by Program Coordinator
   5 min (Speaker: Zdenko Vizintin)
01. Overview of Vaginal Erbium Laser Technology
   15 min (Speaker: Zdenko Vizintin)

PART I – Stress Urinary Incontinence (SUI)

02. Non-ablative Erbium Laser for SUI - European Multi-center Randomized Controlled Trial
   20 min (Speaker: Dr. Neza Koron)
03. Non-ablative Erbium Laser for SUI – Combined Intra-vaginal Plus Intra-urethral Treatment
   20 min (Speaker: Dr. Aleksandra Novakov-Mikic)
04. Q&A of Part I
   8 min (Moderators: Dr. Marco Gambacciani, Zdenko Vizintin)

PART II – Genitourinary Syndrome of Menopause (GSM)

05. Non-ablative Erbium Laser for GSM and Urinary Symptoms of GSM
   20 min (Speaker: Dr. Adrian Gaspar)
06. Non-ablative Erbium Laser for GSM in Breast Cancer Patients and its Effects on Sexual Satisfaction
   20 min (Speaker: Dr. Marco Gambacciani.)
07. Q&A of Part II
   8 min (Moderators: Dr. Aleksandra Novakov-Mikic, Dr. Neza Koron)

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The 29th World Congress on Controversies in Obstetrics, Gynecology & Infertility

PART III –Other Emerging Laser Applications for Women's Health

08. Laser Treatment of Superficial Dyspareunia
    10 min (Speaker: Dr. Marco Gambacciani)
09. Laser Treatment of HPV in Cervical Canal
    10 min (Speaker: Dr. Letitia Lazzaletta)
10. Other Laser Applications in Gynecology
    10 min (Speaker: Zdenko Vizintin)
11. Q&A of Part III
    8 min (Moderators: Dr. Aleksandra Novakov-Mikic, Dr. Neza Koron)

PART IV - Test

12. End-of-Course Test
    10 min

Short Course Description:

Course participants will learn the basic principles of using lasers in a variety of non-surgical and surgical procedures within the fields of minimally invasive gynecology.

The entire course constitutes of twelve topics divided into four parts. In Part I the use of FotonaSmooth Erbium laser systems for Stress Urinary Incontinence will be discussed. The second part is dedicated to laser treatment of Genitourinary Syndrome of Menopause, while in Part III experts will present additional new innovative applications as well as the range of many possible laser treatments. In the last part (IV) participants will have to complete an End-of-Course Test.

Upon completing the End-of-Course Test, the participants will receive the Course Certificate.

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CONTROVERSIES - THE FOUNDATION FOR NEW SOLUTIONS

FRIDAY, DECEMBER 3, 2021

GEDEON RICHTER

10:20-11:50	HALL B
Chairpersons	**Werner Mendling**, *Germany* **Mitchell Creinin**, *USA*
10:20-10:35	RVVC diagnosis and treatment guideline – set up as an ideal **Werner Mendling**, *Germany*
10:35-10:50	RVVC diagnosis and treatment guideline implementation. Facing reality **Peter Greenhouse**, *UK*
10:50-11:05	Discussion
11:05-11:20	VTE risk – from bench to bedside **Mitchell Creinin**, *USA*
11:20-11:35	COCs. The everyday empowerment for women **Rosella Nappi**, *Italy*
11:35-11:50	Discussion

INDIVIDUALIZED PROTOCOLS IN ART

FRIDAY, DECEMBER 3, 2021

GEDEON RICHTER

12:10-13:10	HALL A
Chairperson	**Andreas Tandler-Schneider**, *Germany*
12:10-12:30	Dose adjustment **Raj Mathur**, *UK*
12:30-12:50	Type and dose of gonadotropins in poor ovarian responders: Does it matter? **Christophe Blockeel**, *Belgium*
12:50-13:10	LPS individualization **Dominic Stoop**, *Belgium*

CONTROVERSIES AND CHALLENGES IN RELAPSED OVARIAN CANCER

SATURDAY, DECEMBER 4, 2021

CLOVIS ONCOLOGY

16:00-17:00	HALL B
Chairpersons	**Robert Armbrust**, *Germany* **Jalid Sehouli**, *Germany*
16:00-16:20	Role of surgery in platinum resistant and sensitive relapsed ovarian cancer **Robert Armbrust**, *Germany*
16:20-16:40	Role of maintenance therapy **Radoslav Chekerov**, *Germany*
16:40-17:00	Role of chemotherapy free treatment protocols **Jalid Sehouli**, *Germany*

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Cryos International is the world's largest sperm and egg bank. We offer delivery to over 100 countries, and have more than 1,000 carefully selected donors of many different ethnicities and phenotypes for your patients to choose from.

Quality, compliance, and safety are of utmost importance at Cryos, which is why we are ISO 9001:2015 certified and always committed to meeting the highest quality standards. We offer an easy ordering process as well as fast and reliable shipping, and the ability to register pregnancies online. With more than 30 years of experience and a professional, dedicated team committed to helping others achieve their dreams of becoming parents, you can feel confident in your decision to choose Cryos as your business partner.

CRYOSINTERNATIONAL.COM

Cryos

Industry Profiles

www.besinshealthcare.co.uk

Besins Healthcare is a privately held, global pharmaceutical company headquarter in Monaco. We are a world leader in novel therapies for gynecology and andrology. We have discovered ground-breaking technologies to improve patient well-being throughout our history. We developed several hormone therapies over the years including bioavailable natural progesterone by different routes of administration for pregnant women from conception until delivery and a natural testosterone transdermal gel for testosterone deficiency syndrome. We continue to be a leader in Estradiol Replacement Therapy with the first transdermal gel marketed in Europe. Our products are trusted and prescribed by healthcare professionals in more than 100 countries throughout the world.

www.cegat.de

CeGaT GmbH is a leading global provider of genetic diagnostics and mutation-related disease analyses. The company combines its next-generation sequencing (NGS) process and analysis pipelines with its medical expertise – dedicated to identifying the genetic cause of disease and supporting patient management.
Through NGS, it is possible to analyze all genes associated with a disease phenotype simultaneously – both fast and effectively. An interdisciplinary team of scientists and physicians evaluates the data and summarizes the findings in a comprehensive medical report. All services are performed in-house.
CeGaT, founded in 2009 and based in Tübingen, Germany, is accredited according to CAP, CLIA, and DIN EN ISO 15189:2014.

www.clovisoncology.com

Founded in 2009, **Clovis Oncology** is a commercial stage biotechnology company focused on acquiring, developing and commercializing cancer treatments in the United States, Europe and other international markets. Clovis' product development programs generally target specific subsets of cancer, and the Company seeks to simultaneously develop, with partners, for those indications that require them, diagnostic tools intended to direct a compound in development to the patients most likely to benefit from their use. Through these collaborations, Clovis has the flexibility to choose the most appropriate technology for each program, and the expertise to gain regulatory approvals and support global commercialization that will parallel Clovis' regulatory and commercialization paths.

dk.cryosinternational.com

Cryos International is here to help people on their path to parenthood. We are proud to provide specialized reproductive products, excellent customer care, and personal consultation – and we have done so for over 30 years. Our sperm come from all backgrounds and represents a large variety of ethnicities and phenotypes.
We have computerised systems that have been designed and worked on for over a decade, in order to ensure traceability and security. Furthermore, we are licensed according to the FDA and EU-Tissue Directive, setting the highest standards of quality and safety. For Cryos, it's personal!

www.ferring.com

Ferring Pharmaceuticals is a research-driven, specialty biopharmaceutical group committed to helping people around the world build families and live better lives. Headquartered in Saint-Prex, Switzerland, Ferring is a leader in reproductive medicine and women's health, and in specialty areas within gastroenterology and urology. Ferring has been developing treatments for mothers and babies for over 50 years and has a portfolio covering treatments from conception to birth. Founded in 1950, privately-owned Ferring now employs approximately 6,500 people worldwide, has its own operating subsidiaries in nearly 60 countries and markets its products in 110 countries.

Fertilovit®
for a new life

www.fertilovit.com

Austrian-based **Gonadosan Distribution GmbH** is dedicated to the development and research of state-of-the-art nutraceuticals meeting the specific nutritional needs of men and women planning for pregnancy. The Fertilovit® range of supplements is based on the latest scientific data, tested in cooperation with big European ART centers and has been proven to support fertility treatment effectively. A variety of patent-protected preparations offer highly specific solutions for different male and female fertility patients, ranging from mature patients to patients with thyroid autoimmunity, endometriosis, PCOS, and idiopathic OAT.

Fotona
choose perfection

www.fotona.com

With more then 50 years of experience, **Fotona** is a world-leading medical laser manufacturer recognized for its innovative, award-winning laser systems for applications in gynecology, surgery, aesthetics & dermatology and dentistry.
Fotona's combined Er:YAG and Nd:YAG laser systems are proven to be less invasive and highly effective for clinical and aesthetic gynecology treatments. We are proud to be the first manufacturer to introduce SMOOTH® mode technology for a range of non-invasive laser vaginal treatments.
Our global distribution network spans across more than 90 countries, ensuring comprehensive support and service for Fotona laser users, including clinical training, workshops and hands-on demonstrations.

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www.richter.hu

Gedeon Richter Plc., headquartered in Budapest, Hungary, is a major pharmaceutical company in Central Eastern Europe, with an expanding direct presence in Western Europe, in China and in Latin America. Having reached a market capitalisation of EUR 4.1 billion (USD 4.9 billion) by the end of 2017, Richter's consolidated sales were approximately EUR 1.4 billion (USD 1.6 billion) during the same year. The product portfolio of Richter covers many important therapeutic areas, including Women's Healthcare, Central Nervous System, and Cardiovascular areas. Having the largest R&D unit in Central Eastern Europe, Richter's original research activity focuses on CNS disorders. With its widely acknowledged steroid chemistry expertise, Richter is a significant player in the Women's healthcare field worldwide. Richter is also active in biosimilar product development.

IBSA

Caring Innovation

www.ibsagroup.com

IBSA is an international pharmaceutical company with headquarters in Lugano, Switzerland.
IBSA has developed an entirely new purification process in order to obtain a full range of highly purified, human gonadotrophins (hFSH, hMG and hCG). This patented process ensures both a high level of purity and the full respect of the natural glycosylation of these molecules.
Recently IBSA has marketed a novel ingenious system to deliver progesterone subcutaneously in an aqueous solution.
IBSA has managed to guarantee the highest quality of its products over the years due to the advantages of having a complete in-house manufacturing process in company-owned plants and thanks to a global quality system.
The company's other franchises include osteoarthritis, pain-management, dermatology and thyroid diseases.

www.italfarmaco.com/en-us

Italfarmaco is a private Italian multinational company located in Milan, operating in Italy and abroad in both the pharmaceutical and fine chemical industries through its controlled and/or participated companies. Italfarmaco was established in 1938.
Today Italfarmaco Group markets ethical products in Italy, Switzerland, France, Spain, Germany, Portugal, Greece, Russia, Turkey, Chile, Peru, Morocco and also for its subsidiary company Chemi Spa in USA and Brazil, where it employs over 3000 people. Its products, always with high therapeutic content, are mainly oriented towards the cardiovascular, immuno-oncologic, gynecological, osteoporosis and neurologic area.

www.karlstorz.com

KARL STORZ is a renowned manufacturer that is well established in all fields of endoscopy and can be considered as market leader in rigid endoscopy. The still family held company was founded in 1945 in Tuttlingen, Germany, and has grown to one with a worldwide presence and 8,300 employees. KARL STORZ offers a range of both rigid and flexible endoscopes for a broad variety of applications. Today's product range also includes fully integrated concepts for the OR and servicing.

www.kitazato-ivf.com

Kitazato Corporation is a global company based in Japan, dedicated to the assisted reproductive technologies field.
World leaders in vitrification of human specimens thanks to the development and worldwide implementation of The Cryotop® Method, used by over 2,300,000 professionals a year, we perform extensive research, develop, manufacture and market medical devices and media to support a wide range of fertility treatments on the IVF LifeCycle, from IUI to PGT, including catheters, needles, oils and media.
Our work over the last decades have led Kitazato to become the undisputed market leader in cryopreservation of human gametes.

www.pantarheibio.com **www.pantarheioncology.nl**

Pantarhei Bioscience and Pantarhei Oncology
Pantarhei Bioscience (PRB) and Pantarhei Oncology (PRO) focus on innovative drug development in Woman's Health (WH) and Endocrine Cancers.
PRB has developed a product pipeline based on its ability to identify, confirm and patent protect novel targets and medical uses of existing drugs, hormones, other endogenous human biologicals and combinations thereof. Pantarhei adheres to the highest scientific standards for preclinical and clinical drug development.
The current pipeline of Pantarhei includes (i) Androgen Restored Contraception (ARC), adding dehydroepiandrosterone (DHEA) to oral contraceptives, (ii) the fetal estrogen Estetrol (E4) for the (co)-treatment of breast and prostate cancer and (iii) the use of the Zona Pellucida 3 (ZP3) antigen and biomarker for immunotherapy of ZP3 expressing tumors such as ovarian and prostate cancer.

www.preischool.com

Permanent International and European School in Perinatal, Neonatal and Reproductive Medicine.
Founded in Florence (Italy) in 2012, the School, inspired by the values of scientific culture, ethics and bioethics of life sciences, pursues the aim of promoting and enhancing the fundamental ideals of maternal infant medicine in its entire course: reproductive, periconceptional, maternal and child health periods. The School run courses of reproductive, perinatal and neonatal medicine and related disciplines, training programs, national and international conferences, congresses, debates, and any other event or action consistent with its objectives.

Notes

Fertility

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